STATISTICAL ANALYSIS PLAN

PROTOCOL NO: NCIG-007R

Randomized, Double Blind, Placebo-Controlled Trial of the Efficacy of Intranasal Oxytocin for the Treatment of Alcohol Use Disorder

Protocol Version No.: 4.0 **Version Date:** 5 July 2022

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National Institute on Alcohol Abuse and Alcoholism

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1. ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
AICc	Akaike Information Criterion corrected for finite samples
AUC	Area under the concentration time curve
AUD	Alcohol Use Disorder
BAC	Blood alcohol concentration
BID	Twice daily
BIS	Barratt Impulsiveness Scale
BPAQ	Buss-Perry Aggression Questionnaire
CFR	Code of Federal Regulations
CI	Confidence interval
CIWA-AR	Clinical Institute Withdrawal Assessment for Alcohol-revised
CrCl	Creatinine clearance
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common terminology criteria for adverse events
dL	Deciliter
DSM-5	Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition
DSMB	Data and Safety Monitoring Board
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EDMS	Electronic Data Management System
EOS	End of study
F	Fahrenheit
FA	Full Analysis
FDA	Food and Drug Administration
g	Gram
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
hr	Hour
ICH	International Conference on Harmonization
IDS	Inventory of Drinking Situations
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
µg	Microgram
min	Minutes
MINI	MINI Neuropsychiatric Interview
mL	Milliliter
Mm	Millimeter
NHDD	No heavy drinking days

Abbreviation	Definition
NIAAA	National Institutes on Alcohol Abuse and Alcoholism
Oz	Ounce
POMS	Profile of Mood State
PSNHDD	Percentage of subjects with no heavy drinking days
PT	Preferred term
RNA	Ribonucleic acid
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SDU	Standard drinking unit
SNAQ	Simplified Nutritional Appetite Questionnaire
SOC	System Organ Class
STAI	Spielberger Trait Anxiety Inventory
THC	Tetrahydrocannabinol
TLFB	Timeline followback
ULN	Upper limit of normal
WHO	World Health Organization

2. INTRODUCTION

This statistical analysis plan (SAP) for Protocol No. NCIG-007R, "Randomized, Double Blind, Placebo-Controlled Trial of the Efficacy of Intranasal Oxytocin for the Treatment of Alcohol Use Disorder" describes and expands upon the analytical plan presented in the protocol.

This document contains all planned analyses, reasons and justifications for these analyses for all study data. This plan also includes sample tables, figures, and listings that will be populated. The SAP will follow the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines as indicated in Topic E3 (Structure and Content of Clinical Study Reports), Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA) and ICH.

The following sources were used in preparation of this SAP:

- Protocol # NCIG-007R, Protocol Version No.: 4.0; Version Date: 05Jul2022
- ICH Guidance Topics E9, E3 and E8

3. PROTOCOL SUMMARY

3.1 Study Objectives

3.1.1 Primary

The primary objective of the study is to compare the efficacy of intranasal oxytocin in reducing the weekly percentage of heavy drinking days over the 10 weeks of maintenance treatment among subjects with moderate to severe Alcohol Use Disorder (AUD). A "heavy drinking day" is 4 or more drinks per drinking day for women and 5 or more drinks per drinking day for men.

3.1.2 Secondary

Secondary objectives include assessment of other measures of the effects of oxytocin compared with placebo on reduction of alcohol use as well as effects on alcohol craving, alcohol-related consequences, cigarette smoking and other nicotine use, psychological assessments, retention in the study, and safety and tolerability throughout the study.

3.2 Study Design

This study is a double-blind, randomized, placebo-controlled, parallel group, multi-site clinical trial designed to assess the efficacy of oxytocin compared with placebo to reduce drinking in 100 subjects (50 in each group) who report 4 or more Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5™) symptoms of AUD. This study will be conducted at 4 clinical sites. If eligible for the study, subjects will be randomized using a stratified permuted block randomization procedure with "clinical site" as a stratification variable in an approximate 1:1 ratio (targeting 50 subjects per group) to receive either intranasal oxytocin or placebo for 12 weeks.

If eligible for the study, subjects will receive blinded intranasal oxytocin at 35 IU once per day or intranasal placebo (same volume once per day) for 2 weeks (initial tolerability assessment period), then for the next 10 weeks (maintenance period) subjects will receive oxytocin at 35 IU/ twice per day (BID, totally daily dose 70 IU) or intranasal placebo (same volume twice per day)

Subjects will be seen in the clinic at screening visit(s), at randomization, and at Weeks 2, 3, 4, 6, 8, 10, and 13. During the alternate weeks when subjects will not be coming into the clinic (Weeks 5, 7, 9, 11, and 12), subjects will be contacted once during that week by telephone to encourage study drug compliance and to assess withdrawal, adverse events (AEs), and concomitant medication use. A final follow-up telephone interview will occur during Weeks 14/15 (1-to-2 weeks after the end of dosing).

Enrollment will be halted if 2 or more at least possibly related SAEs as judged by the investigator or medical monitor occur. If this occurs, a DSMB meeting will be convened and a decision, in conjunction with the study Sponsor, will be made regarding stopping the study.

The overall study schema is provided in Figure 1. The study schedule of visits and assessments is shown in Table 1.

Figure 1. Overview of Study Design

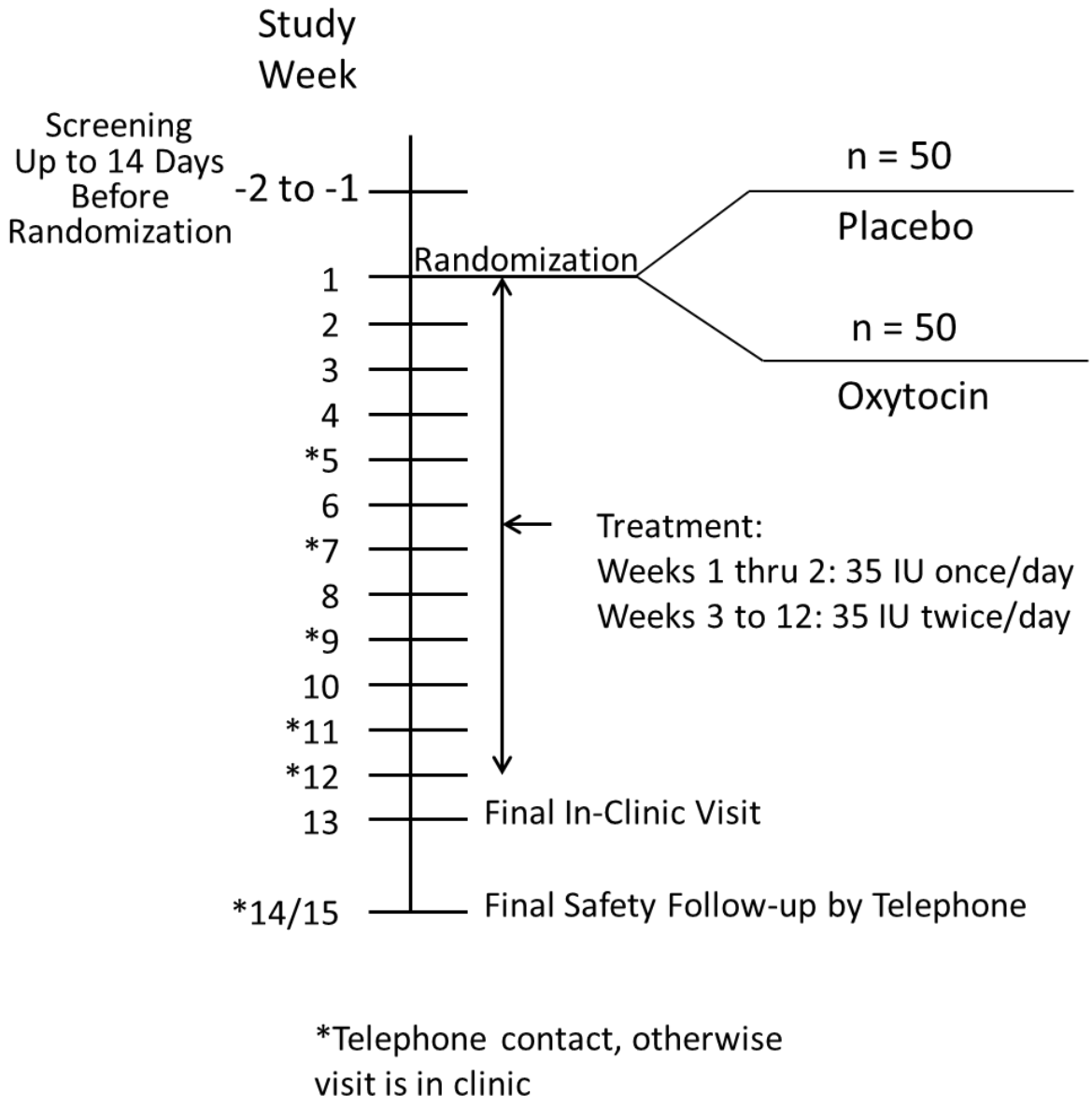

Table 1. Schedule of Assessments

	Screen			Maintenance										EOS[a]	Safety Follow-up
Study Week	**-2 to -1**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14/15**
Clinic Visit #	**1**	**2**	**3**	**4**	**5**		**6**		**7**		**8**			**9**	
Informed Consent	X														
Alcohol Breathalyzer	X	X	X	X	X		X		X		X			X	
Urine Drug Screen[b]	X	X	X	X	X		X		X		X			X	
Locator Form	X														
Demographics	X														
Medical/Surgical History	X	X[c]													
Physical Exam	X[d]	X	X	X	X		X		X		X			X	
MINI V 7.0.2 (AUD module at EOS)	X													X	
C-SSRS		X	X				X		X		X			X	
Clinical Chemistry[e]	X						X		X		X			X	
Vital Signs	X	X	X	X	X		X		X		X			X	
ECG (12-lead)	X													X	
Prior and Concomitant Meds	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CIWA-AR	X	X	X	X	X		X		X		X			X	
Eligibility Checklist	X	X[c]													
Drug Compliance – Diary review		X	X	X	X		X		X		X			X	
Drug Accountability (vial weight)		X	X	X	X		X		X		X			X	
Pregnancy Test/Female Birth Control Methods	X	X	X[f]				X		X		X			X	
Weight	X						X		X		X			X	
Drinking Goal	X														
AEs/SAEs			X	X	X	X	X	X	X	X	X	X	X	X	X
Other Services Used for Alcohol Use Problems[g]		X												X	
RANDOMIZATION		X													
Brief Telephone Interview[h]						X		X		X		X	X		
Take Control		X	X	X	X		X		X		X				
Exit Interview														X	
Treatment Referral														X	
Follow-Up Telephone Interview															X
Final Subject Disposition															X
Subject Reported Outcomes															

	Screen			Maintenance										EOS[a]	Safety Follow-up
Study Week	**-2 to -1**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14/15**
Clinic Visit #	**1**	**2**	**3**	**4**	**5**		**6**		**7**		**8**			**9**	
Hyperkatifeia Scale		X												X	
Barrett Impulsivity Scale		X													
Spielberger Trait Anxiety Inventory		X													
BPAQ - SF[i]		X					X		X		X			X	
Simplified Nutritional Appetite Questionnaire		X					X		X		X			X	
Cigarette and other nicotine use		X					X		X		X			X	
ECR-RS[j]		X					X		X		X			X	
IDS-30[k]		X													
POMS		X					X		X		X			X	
PROMIS – alcohol negative consequences		X					X		X		X			X	
PROMIS – sleep disturbances		X					X		X		X			X	
PROMIS – pain interference		X					X		X		X			X	
UPSIT[l]		X		X			X		X		X			X	
Urge to drink questionnaire		X					X		X		X			X	
Timeline followback (TLFB)	X	X	X	X	X		X		X		X			X	
Brief Drinking Questionnaire[m]														X	

[a] EOS=end of study. These assessments are to be done at Week 13 or if the subject discontinues early and agrees to a final clinic visit.

[b] Test for opioids, cocaine, amphetamines, methamphetamine, THC, buprenorphine, methadone, benzodiazepines, oxycodone, 3,4-methylenedioxy-methamphetamine (MDMA), and barbiturates.

[c] Updated prior to randomization.

[d] Complete physical exam at screening including examination of the nares, plus examination of the nares at all other visits as indicated.

[e] AST, ALT, total bilirubin, creatinine, sodium, and potassium.

[f] Only birth control methods are collected at this visit.

[g] At baseline asks about lifetime treatment use and at EOS asks “since beginning this study”

[h] AEs, concomitant medications, and drug compliance reminder.

[i] Buss Perry Aggression Questionnaire – Short Form

[j] Experiences in Close Relationships—Relationship Structures Questionnaire (ECR-RS) (attachment related anxiety)

[k] Inventory of Drinking Situations

[l] University of Pennsylvania Smell Identification Test

[m] Only asked to subjects who request to withdraw from the study and are not willing to provide TLFB drinking data. This questionnaire will be asked at whatever constitutes the EOS visit.

3.3 Study Endpoints

3.3.1 Primary Efficacy Endpoint

The primary efficacy endpoint is the weekly percentage of heavy drinking days during the 10 week maintenance period (study weeks 3-12). A "heavy drinking day" is 4 or more drinks per drinking day for women and 5 or more drinks per drinking day for men.

3.3.2 Secondary Efficacy Endpoints

Secondary endpoints that will be analyzed during the 10-week maintenance period (study weeks 3-12)include:

1. Percentage of subjects with no heavy drinking days during treatment
2. Percentage of subjects abstinent from alcohol during treatment
3. Percentage of subjects with a WHO drinking risk category decrease during treatment of:
    a. At least 1-level
    b. At least 2-levels
4. Endpoints analyzed monthly and with 1- and 2-month grace periods:
    a. Percentage of subjects with no heavy drinking days during the period
    b. Percentage of subjects abstinent from alcohol during the period
    c. Percentage of subjects with WHO drinking risk category decrease during the period of:
        – at least 1 level
        – at least 2 levels
5. Percentage of days abstinent per week
6. Weekly mean number of drinks per week
7. Weekly mean drinks per drinking day
8. MINI AUD symptoms at end of study
9. Cigarettes smoked per week among smokers
10. Abstinence from cigarette smoking
11. Days used other nicotine products per week
12. Abstinence from nicotine use
13. Experiences in Close Relationships—Relationship Structures Questionnaire (ECR-RS) (attachment related anxiety)
14. PROMIS – alcohol-related negative consequences
15. PROMIS – sleep disturbances
16. PROMIS – pain interference

17. Profile of Moods States (POMS) (including subscales)
18. Urge to Drink Scale (UDS)

3.3.3 Exploratory Efficacy Endpoint

Hyperkatifeia Scale score at end of study

3.3.4 Safety Endpoints

Safety endpoints will be analyzed over the entire treatment and follow-up period.

1. Vital signs
2. Physical examination of the nasal mucosa
3. Smell testing with the University of Pennsylvania Smell Identification Test (UPSIT)
4. Blood chemistries
5. Urine drug screen results
6. Blood alcohol concentration (BAC) by breathalyzer
7. AEs/SAEs
8. Electrocardiogram (ECG) results
9. Clinical Institute of Withdrawal - Alcohol Revised (CIWA-AR) scores
10. Frequency of subjects with suicidal ideation at any time during the treatment period - Columbia-Suicide Severity Rating Scale (C-SSRS)
11. Change in appetite - Simplified Nutritional Appetite Questionnaire (SNAQ) scores and percentage of subjects with SNAQ scores ≤14.
12. Buss-Perry Aggression scores (BPAQ)

3.3.5 Compliance

Compliance will be assessed using the Subject Diary and by weighing the used study drug vials prior to and after use to calculate the amount dispensed.

4.0 DEFINITION OF ANALYSIS SETS

The study analysis populations will consist of the following:

Full Analysis (FA) Set: The full set is defined as subjects randomized to participate in the study who took at least one dose of investigational product. The full analysis set will be used to evaluate all efficacy and safety endpoints.

5.0 ASSESSMENT AND JUSTIFICATION OF STUDY ENDPOINTS

5.1 Alcohol Consumption Endpoints

5.1.1 Daily Quantity of Alcohol Consumption

Drinking will be assessed using the TLFB methodology (Sobell et al., 1992). The TLFB is a semi-structured interview that provides estimates of the daily quantity of alcohol consumption during specified time periods. It uses a calendar prompt and a number of other memory aids (e.g., holidays, payday, and other personally relevant dates) to facilitate accurate recall of drinking or other drug use during the target period. The procedure has been widely used in clinical and research contexts. It has demonstrated adequate levels of reliability and validity when administered as an in-person interview, over the telephone, and when administered via computer (Carey 1997; Sobell et al., 1988; Sobell et al., 1996).

After consent is signed, the TLFB interview will be performed for the 28-day period prior to signing consent. Thereafter, the interview will be for the previous days between the last assessment and the day prior to the day of the assessment.

If a subject requests to withdraw from the study but agrees to continued telephone contact to assess drinking, the TLFB will be performed over the phone for the duration of the study at a frequency acceptable to the study subject and site staff.

5.1.2 Drinking Days

A drinking day is one calendar day in which the subject reported any alcohol consumption (i.e., > 0 standard drinking units [SDUs]). A standard drink contains approximately 0.6 fluid ounces (oz) of pure alcohol. The data given by the subjects on amount and type of alcoholic beverage(s) consumed will be converted to SDUs. An Excel spreadsheet customized for use in this study will be used for double data entry by clinical site staff to collect the TLFB drinking data. This spreadsheet contains a calculator to determine standard drink units (SDUs). Standard drink unit definitions are provided in Table 2.

Table 2: Standard Drink Unit Definitions

For Beer (~ 5% alcohol), the approximate number of SDUs in: • 12 oz = 1.0 • 16 oz = 1.3 • 24 oz = 2.0 • 40 oz = 3.3 For malt liquor (~ 7% alcohol), the approximate number of SDUs in**:** • 12 oz = 1.4 • 16 oz = 1.9 • 22 oz = 2.6 • 40 oz = 4.7
For table wine (~ 12% alcohol), the approximate number of SDUs in: • 750 mL bottle = 25oz = 5.0 • 5 oz glass = 1.0

• 10 oz glass = 2.0
For 80 proof spirits (~ 40% alcohol), or hard liquor, the approximate number of SDUs in: • 1.5 oz (mixed drink) = 1.0 • 12.7 oz (pint) = 8.5 • 25 oz (a fifth)= 17.0 • 1.75 L (59 oz) = 39.0

5.1.3 Heavy Drinking Day

A heavy drinking day is defined as a day with 5 or more drinks (SDUs) for males and 4 or more drinks (SDUs) for females.

5.1.4 Days at Risk

If a subject is being treated at an inpatient facility, is incarcerated, or otherwise under confinement, each day spent in under these conditions is considered a reduction in the days at risk for drinking and is deducted from the denominator in calculations of rates of drinking days.

5.1.5 Weekly Percentage of Heavy Drinking Days and Weekly Percentage of Days Abstinent

Weekly percentage of heavy drinking days is the number of heavy drinking days in a 7-day period divided by 7 then multiplied by 100. The TLFB permits capturing data in a subsequent visit if a visit is missed; however, if fewer than 7 days are observed, then the denominator is the number of days observed in the 7-day period. At least 3 days in a week must be observed; otherwise, the week is considered missing.

Weekly percentage of days abstinent is similarly calculated by using the number of days abstinent instead of the number of heavy drinking days.

5.1.6 Percentage of Subjects with No Heavy Drinking Days and the Percentage of Subjects Abstinent from Alcohol

The percentage of subjects with no heavy drinking days is the number of subjects that have no heavy drinking days during the period of interest divided by the number of subjects with at least one day of non-missing drinking data during the period of interest, multiplied by 100.

The percentage of subjects abstinent from alcohol is calculated similarly, except the numerator is the number of subjects that have no drinking days during the period of interest.

5.1.7 Weekly Mean Number of Drinks and Weekly Mean Number of Drinks per Drinking Day

Weekly mean number of drinks is the sum of SDUs calculated to the tenths over 7 calendar days divided by the number of days with non-missing data. The quotient is multiplied by 7. At least 3 days in a week must be observed; otherwise, the week is considered missing.

Weekly mean number of drinks per drinking days utilizes the same numerator, and the denominator is the number of days with greater than 0 SDUs. Weeks where all days within the week are abstinent are assigned a value of 0 for weekly drinks per drinking day.

5.1.8 World Health Organization Drinking Risk Categorical Scale

The WHO has developed a drinking risk categorical scale that can be used in a responder analysis approach to assess clinically relevant decreases in alcohol consumption (Aubin et al, 2015). Two dichotomous endpoints will be analyzed: WHO 1-level and WHO 2-level decrease in alcohol consumption. The WHO 1-level and 2-level decrease endpoints are the percentage of subjects experiencing at least a 1-level or 2-level decrease in WHO levels of alcohol consumption, respectively, from the level at baseline (the period including the 28 days before screening) to the level during period of interest. The WHO levels of average alcohol consumption per day are as follows:

	Males	**Females**
Low Risk	1 to 40g	1 to 20g
Medium Risk	41 to 60g	21 to 40g
High Risk	61 to 100g	41 to 60g
Very High Risk	101+g	61+g

where 14g = 1 SDU (WHO2000). In computing the alcohol consumption level, average drinks per day will be used, computed as the sum of all drinking in the 28 day period divided by the number of days with non-missing drinking data in that period. Abstinent subjects will be included in a separate "Abstinent" category. A subject must have at least 1 week of data during a month to be considered non-missing.

5.2 Alcohol Use Disorder (MINI Version 7 – DSM5)

The AUD module of the MINI Neuropsychiatric Interview (MINI) specifies the severity of AUD into 3 categories based on the total number of symptoms to which the subject is coded "Yes" as follows:

Mild = 2 to 3 symptoms

Moderate = 4 to 5 symptoms

Severe = 6 or more symptoms

Subjects must have at least 4 symptoms to be eligible to participate in the study. The total number of symptoms being scored is 11. No imputation for missing values will be used.

5.3 Barrett Impulsiveness Scale

The Barratt Impulsiveness Scale (BIS) is a questionnaire designed to assess the personality/behavioral construct of impulsiveness. It is a 30-item scale with items scored on a 4-point scale (1=rarely/never; 2= occasionally; 3=often; 4=almost always/always). Items 1, 7, 8, 9, 10, 12, 13, 15, 20, 29, and 30 are reverse scored. The total score is the sum of the individual items. Separate subscale scores for Self-Control and Impulsive behavior will also be calculated. The BIS is among the baseline assessments that are performed only at Week 1.

5.4 Smoking and Cigarettes Smoked per Week

A quantity frequency interview at baseline and during treatment will include two questions to assess cigarette smoking behavior: 1) Over the past week, on how many days did you smoke cigarettes?; and 2) On the days you smoked during the past week, how many cigarettes did you smoke on average? At baseline subjects that answer "0" to question #1 are considered non-smokers for the study. Cigarettes per week is the answer to question #2 multiplied by the answer to question #1. No imputation for missing values will be used.

5.5 Nicotine use and Days of Other Nicotine Use per Week

The cigarette smoking questionnaire will include a third question: 3) Over the past week, on how many days did you use other nicotine products (ex. chew, cigars, cigarillos, e-cigarettes, vape, gum, patch, etc...). A subject is positive for any nicotine use if the number of smoking days or the number of any other nicotine use days is greater than zero.

5.6 Experiences in Close Relationships – Relationship Structures Questionnaire (ECR-RS)

The Experiences in Close Relationships-Relationship Structures scale (Farley et al, 2011) is a questionnaire assessing two-dimensional relationship-specific attachment structures in adults beyond the traditional focus on romantic relationships. This is a 36-item questionnaire, of which only the first 18-item attachment-related anxiety scale will be assessed and evaluated. The presentation of the items were randomized on the form for subject completion. Each item is rated on a 7-point scale where 1 = strongly disagree and 7 = strongly agree. The attachment-related anxiety is determined by averaging the scores of these 18 items. However, items 9 and 11 are "reverse keyed".

5.7 Hyperkatifeia

Hyperkatifeia is defined as a greater intensity of negative emotional/motivational signs and symptoms during withdrawal from drugs of abuse in the withdrawal/negative affect stage of the addiction cycle (Koob 2021). Hyperkatifeia or negative emotional state is considered to be one of stages of addiction in the context of drug withdrawal (Koob and Le Moal 1997, Koob 2019). NIAAA has developed a 24-item self-report Hyperkatifeia Scale to capture negative emotionality after stopping alcohol drinking that will be assessed for the first time in this study of heavy drinkers with a diagnosis of moderate to severe AUD. The items address four measures associated with negative emotional state including anxiety, depression, stress, irritability and pain. Each item is is 5-point Likert scale assessing the intensity of the feelings and sensations experienced when not drinking alcohol. Higher scores are indicative of greater intensity of hyperkatifeia.

5.8 Inventory of Drinking Situations (IDS-30)

The IDS-30 is a 30-item patient completed questionnaire of reward and relief drinking that asks subjects to rate the frequency (0= never, 3 = almost always) of heavy drinking in various situations over the past year (Mann et al, 2018). Fifteen items measure reward drinking

tendencies and 15 items measure relief drinking tendencies. A subsequent evaluation of IDS-30 refined the definition of reward drinking to five items and relief drinking to five items (Votaw et al, 2022)

The reward drinking score is determined by summing the scores for these items: 6, 18, 21, 23, 27.

The relief drinking score is determined bu summing the scores for these items: 9, 14, 15, 22, 25

Missing data is not imputed. All five questions within each scale must be answered for a score to be computed; otherwise, the scale is missing.

5.9 PROMIS Questionnaires

PROMIS® (Patient-Reported Outcomes Measurement Information System) is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children that were developed through the support of U. S. Department of Health and Human Services (https://www.healthmeasures.net/explore-measurement-systems/promis). Three of these assessments, described below, will be utilized in this study.

5.9.1 PROMIS – Alcohol-related Negative Consequences

For negative consequences for alcohol use, the PROMIS Alcohol Negative Consequences – Short Form 7a questionnaire will be used to assess outcomes of alcohol use over the past 30 days. Each of the 7-items assesses the frequency of the negative alcohol-related consequence on 5-point Likert scale with higher scores indicating greater frequency. The scoring manual will be used to compute T-scores for each evaluation. All 7 questions must be answered for the form to be considered non-missing.

5.9.2 PROMIS – Sleep Disturbances

For assessment of subject's sleep quality, the PROMIS Sleep Disturbance – Short Form 8b will be used. The questionnaire consists of 8 questions regarding the quality of sleep over the past 7 days. Each item on the measure is rated on a 5-point scale with a range of scores from 8 to 40 with higher scores indicating greater severity of sleep disturbance. The American Psychiatric Association has established levels of severity (none to slight [<55], mild [55.0 – 59.9], moderate [60 – 69.9] or severe [70 or higher] based on the T-score derived from a conversion table) {add reference to APA website|. At least 5 questions must be answered to be considered non-missing.

5.9.3 PROMIS – Pain Interference

For the assessment of pain interference, the shortened 8a version of the PROMIS for pain interference will be used to measure the self-reported consequences of pain over the past 7 days. This 8-item questionnaire assesses the degree to which pain interferes with various activities. Each item on the measure is rated on a 5-point scale with higher scores indicating greater pain

interference. The scale ranges from 8 to 40. The scoring manual will be used to compute T-scores for each evaluation. At least 5 questions must be answered to be considered non-missing.

5.10 Profile of Mood States (POMS)

The POMS measures dimensions of affect or mood (McNair and Heuchert 2005). It consists of 65 adjectives to which the subject responds according to a 5-point scale ranging from "not at all (0)" to "extremely (5)." Six subscale scores will be computed for items grouped as follows: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment. A Total Mood Disturbance score will also be computed which consists of the sum of Tension-Anxiety, Depression-Dejection, Anger-Hostility, Fatigue-Inertia, and Confusion-Bewilderment scores then subtracting the Vigor-Activity subscale score. A missing value within a subscale will be replaced by the average score of the answered items within the subscale; if 2 or more items within a subscale are missing then the entire subscale will be considered missing.

5.11 Urge to Drink Scale (UDS)

The UDS is a modified version of an assessment that was developed and validated by researchers at the University of Pennsylvania's Center for Studies of Addiction. This measure has been shown to be a valid and reliable instrument for assessing an individual's urge to drink alcohol. This scale has 5 items with 7 different responses to each item scored as 0 to 7. The questions pertain to the past week. The total score is the sum of the point scores for the individual items. Total scores of 10 or higher during treatment have been reported to be associated with increased risk for relapse. Missing values will not be imputed.

6.0 HYPOTHESES TO BE TESTED

6.1 Primary Efficacy Endpoint

It is hypothesized that oxytocin, as compared to placebo will reduce the weekly percentage of heavy drinking days over the 10-week maintenance period (study weeks 3-12). This hypothesis will be tested using other time periods during treatment.

6.2 Secondary Efficacy Endpoints

Over the 10-week maintenance period (study weeks 3-12), it is hypothesized that the oxytocin group, as compared to the placebo group, will:

1. Increase the percentage of subjects with no heavy drinking days
2. Increase the percentage of subjects abstinent from alcohol
3. Increase the percentage of subjects with a WHO drinking risk category decrease of:
    a. 1-level
    b. 2-levels
4. Increase the percentage of days abstinent per week

5. Decease the weekly mean number of drinks per week
6. Decrease the weekly mean drinks per drinking day
7. Decrease the number of MINI AUD symptoms
8. Decrease the cigarettes smoked per week among smokers
9. Increase the smoking abstinence rate among smokers
10. Decrease the weekly number of days of other nicotine use among other nicotine users
11. Increase the nicotine use abstinence rate among nicotine users (includes cigarettes)
12. Decrease in attachment related anxiety scores of the ECR-RS (attachment related anxiety)
13. Decrease in PROMIS sleep disturbance, alcohol-related negative consequences, and pain interference scores
14. Decrease in POMS subscales total mood disturbance, anger-hostility, fatigue-inertia, confusion-bewilderment, tension-anxiety and depression scores and/or increase vigor-activity
15. Decrease in the Urge to Drink scale scores

7.0 SAMPLE SIZE CONSIDERATIONS

With an intake sample of 100 subjects (50 subjects per arm) and 12% attrition, it is projected that the sample size for primary endpoint analyses will be 88 (44 subjects per arm). The alpha level for the primary analyses will be 0.05, two-tailed. An estimate of the effect size (Cohen's d) for the investigational products is 0.60. Equal variances in both groups are assumed. These assumptions lead to a projected power of 0.80.

8.0 DATA QUALITY ASSURANCE

Data quality assurance will start with training of clinical investigative staff on data collection and assessment procedures including a Manual of Operations that describes what data to collect and procedures for completion of electronic case report form (eCRFs.) Completed eCRFs will be reviewed by Fast-Track Drugs and Biologics clinical monitors on a regular basis throughout the trial by comparison against the source documents.

All study data will come from the eCRFs and no other source data. eCRFs for this study were created using an electronic data management system (EDMS) based on Merge eClinicalOS. eCRFs were created using an established data dictionary for each variable including the field name, field type, field attributes, and coding for variables. Range checks, alpha-numeric requirements, and null/not null parameters were programmed as applicable. The back end database application is Oracle. Data entered into the EDMS system will be reviewed by Fast-Track clinical monitors and data managers. If incomplete or inaccurate data are found, the data will be queried in the system for site staff to address. The site will resolve data inconsistencies and errors using the EDMS with full audit trail of corrections being maintained within the

system. Corrections and changes to the data will be reviewed by Fast-Track clinical monitors and data managers.

Additional edit checks will be written to detect anomalies in the database. These checks will address inconsistencies (within visits, across visits), invalid/unusual values, missing values, and protocol violations. Edit checking will be validated on test data or actual clinical trial data. In addition to programmed edit checks, quality control examination of data will also be performed on reviews of data listings.

9.0 STATISTICAL CONSIDERATIONS

9.1 General Considerations

For descriptive purposes, dichotomous and categorical variables will be presented as number of observations and percentages; continuous variables will be given as means, standard deviations (SD), median, minimum (min) and maximum (max). Statistical tests will be two-tailed at a 0.05 Type I error rate. P-values for the primary and secondary endpoints of < 0.05 will be considered statistically significant. Endpoint data will also be screened for outliers and skewness. Appropriate non-parametric tests will be used to compare treatment groups on continuous baseline characteristics that are not normally distributed. Continuous endpoint data that are not normally distributed will be transformed using either a square root, logarithmic, or inverse transformation, the selection of which is determined by skewness and kurtosis statistics with values closest to zero and normalization of histograms. Cohen's d will be used to calculate the effect size for means. Odds ratios will be provided for all dichotomous outcomes. Descriptive statistics – mean, SD, median, min and max – of all endpoint data will be provided for each assessment point or summarized at each week for drinking endpoints. All data will be presented in listings. All analyses will be performed in the full analysis set.

9.2 Participant Accountability and Protocol Deviations

A summary will be prepared to show dropouts/retention over time in each group, along with the reason for early termination. The number of missing observations will be presented between groups. Protocol deviations will be presented as summaries by type of deviation.

9.3 Demographics and Other Baseline Characteristics

Summaries of the characteristics of the subjects in each of the study groups at baseline will be prepared for the full analysis set. Demographic characteristics (e.g., age, gender, race, and ethnicity) and other baseline characteristics including Barratt Impulsiveness scale (BIS), mood scales (e.g., Spielberger Trait Anxiety Inventory (STAI), Buss-Perry Aggression Questionnaire (BPAQ), POMS total and subscale scores), hyperkatifeia questionnaire, ECR-RS, Simplified Nutritional Appetite Questionnaire (SNAQ), PROMIS scales for alcohol negative consequences, sleep disturbances, and pain interference, University of Pennsylvania Smell Identification Test (UPSIT), and drinking goal) will be summarized by treatment group.

Baseline drinking parameters in the 28-days prior to the start of screening, age started drinking regularly, medical treatments for drinking in the past year, and other services used for alcohol problems in the past 4 weeks prior to consent will be summarized by treatment group. The

number and percentage of subjects with mild, moderate and severe symptoms of AUD and summary statistics for total number of symptoms will also be presented.

The numbers and percentages of subjects who are smokers, used any nictonine, used any other nicotine products, and any THC will be presented. The quantity of cigarettes smoked per week will be presented among smokers, and the number of days of other nicotine products used per week will be presented among subjects with any other nicotine product use.

Baseline drinking-associated consequences (CIWA-AR), alcohol craving (Urge to Drink Scale) total score, and Inventory of Drinking Situations (IDS) subscales of reward drinking and relief drinking will be summarized in a table.

Continuous variables will be summarized using means, standard deviations, medians, min, and max values. Categorical variables will be summarized using counts and percentages.

The comparability among the treatment groups with respect to the demographic and baseline variables will be evaluated by appropriate statistical methods. These will include t-tests for continuous variables, chi-square tests for categorical variables, and Fisher's exact test for binary variables. If a continuous variable is skewed, then the Wilcoxon rank sum test will be used on the raw data or a t-test on an appropriately transformed variable.

9.4 Efficacy Analysis

9.4.1 Primary Analysis of Primary Efficacy Endpoint

The primary efficacy endpoint is the weekly percentage of heavy drinking days during the 10-week maintenance period (study weeks 3-12). The primary analysis of the primary endpoint will be a fully covaried, mixed-effect model for repeated measures employed on the Full Analysis Set (using an appropriate transformation of the endpoint, if needed; see Section 9.1). Treatment group, study week, treatment group by study week interaction, clinical site and baseline percentage of heavy drinking days will be covariates in the mixed effects model. The analyses will be performed using SAS PROC MIXED procedure Subjects are treated as a class variable and not continuous. The week, treatment group, and clinical site are also treated as class variables. Additional covariates may be selected using the method described in Section 9.4.3.The solution statement from SAS PROC MIXED is requested to provide the solution for the fixed effects parameters. A REPEATED statement specifies that values are repeated each week and subjects are nested within treatment group. The covariance structure is specified.

The selection of the covariance structure is performed using a simple repeated mixed effects model that includes treatment group as the only fixed effect and subject nested within treatment group as the only random effect. The covariance structure is selected from autoregressive, compound symmetry, Toeplitz, and unstructured. The Akaike Information Criterion (AICc) corrected for a finite sample is obtained from each of the four models for the four possible covariance structures to determine model fit. The smallest (minimum) AICc associated with one of the covariance structures is selected and the difference for each of the other three covariance structures is calculated. A graph is produced of the model fit statistics and relative difference for the four possible covariance structures.

If the primary endpoint requires a transformation, another mixed effect model that is identical to the primary analysis model will be run using the untransformed endpoint. Results based on the primary analysis model and the model of the untransformed endpoint will be presented in tabular form. The overall least squares means and least square means for each time point along with the 95% confidence intervals (CI) will be presented for the untransformed endpoint only (for descriptive purposes), while two-tailed p-values and Cohen's d will be presented for both the untransformed and transformed data. Inference and Cohen's d will be based upon the results using appropriately transformed data. A graph of the primary endpoint will be produced using the LSMEANs from the untransformed endpoint with p-values and Cohen's d comparing weekly differences obtained from the appropriately transformed variable.
Descriptive statistics will be reported for all study weeks (1-12) by treatment group.

9.4.2 Analysis of Secondary Endpoints

Continuous secondary efficacy endpoints with repeated measures will also be analyzed based on data collected during the treatment period, including TLFB and other questionnaire data assessed at Week 13 that reflect data collected during this period.

In general, every continuous secondary efficacy endpoint with repeated measures is analyzed using a repeated measures mixed effects model as discussed in Section 9.4.1. Results will be presented using the same tabular and graphical formats detailed in Section 9.4.1.The primary analysis model is:

appropriately transformed endpoint = treatment + week + treatment*week + clinical site + baseline equivalent of endpoint + other covariates (identified in Section 9.4.3).

It is anticipated that the covariance structure selected for the primary endpoint will also be used for secondary endpoints; however, the selection process detailed in Section 9.4.1 will be followed for each continuous secondary endpoint.

The primary analysis model for continuous endpoints measured at one time is a general linear model (GLM): appropriately transformed endpoint = treatment + clinical site + baseline equivalent of the endpoint + other covariates (identified in Section 9.4.3).

The primary analysis model for dichotomous endpoints is a logistic regression model that includes treatment + clinical site + other covariates (identified in Section 9.4.3). If fewer than 5 events are observed for a dichotomous endpoint then no logistic regression will be performed. In this situation Fisher's exact test will be used to compare treatment groups.

All analyses of secondary endpoints will use the Full Analysis Set.

Descriptive statistics of all secondary endpoints will be reported for all study weeks (1-12) or times at which they were measured within the treatment period, by treatment group.

9.4.2.1 Secondary Drinking Endpoints

The continuous endpoints – percentage of days abstinent per week, weekly mean number of drinks per week, and weekly mean number of drinks per drinking day – will be analyzed using the mixed effects model specified in Section 9.4.2. Covariates for these models will be identified as in Section 9.4.3.

The dichotomous endpoints –percentage of subjects with a WHO 1-level decrease, and WHO 2-level decrease in alcohol consumption risk category, percentage of subjects with no heavy drinking days, and percentage of subjects abstinent from alcohol – will be assessed for the entire 10-week maintenance period, with 1- and 2-month grace periods, and Month 2 and Month 3. These endpoints will be analyzed with the logistic regression model specified in Section 9.4.2. Covariates for these models will be identified as in Section 9.4.3.

9.4.2.2 Alcohol Use and Craving Endpoints

The MINI AUD module is assessed at screening and Week 13. The number of AUD symptoms at Week 13 is a continuous variable and will be modeled using a GLM specified in Section 9.4.2. Covariates for these models will be identified as in Section 9.4.3.
Craving is assessed using the Urge to Drink Scale which is assessed repeatedly during the treatment period. The total score will be analyzed using the mixed effect model approach detailed in Section 9.4.2. Covariates for this model will be identified as in Section 9.4.3.

9.4.2.3 Psychosocial Endpoints

The POMS, ECR-RS, and the three PROMIS scales (including negative alcohol-related consequences, sleep disturbance, and pain interference) are continuous variables assessed repeatedly throughout the treatment period. The POMS includes the overall Total Mood Disturbance and other subscales, and each will be individually analyzed. The ECR-RS is a 36-item questionnaire of which only the first 18-item attachment-related anxiety scale will be assessed and analyzed. The three PROMIS scales employed in this study will be transformed into T-scores prior to analysis. The POMS, ECR-RS and PROMIS scores will be analyzed using the mixed effect model approach detailed in Section 9.4.2. Covariates for these models will be identified as in Section 9.4.3.

9.4.2.4 Nicotine-Related Endpoints

The dichotomous endpoints – abstinence from smoking and abstinence from nicotine use – will be analyzed with the logistic regression model described in Section 9.4.2. Covariates for these models will be identified as in Section 9.4.3.

The mean number of cigarettes smoked in the past week is a continuous variable measured repeatedly during the treatment period. This endpoint will be analyzed only for those subjects who smoked at baseline. The data will be analyzed using the mixed effects described in Section 9.4.2. Covariates for this endpoint will be identified in Section 9.4.3.

The mean numbers of days of other nicotine product use is a continuous variable measured repeatedly during the treatment period. This endpoint will be analyzed only for those subjects who used other nicotine products at baseline. The data will be analyzed as described in Section 9.4.2. Covariates for this endpoint will be identified in Section 9.4.3.

9.4.3 Covariate Adjustment for the Analysis of Endpoints

Covariates for the continuous efficacy endpoints measured repeatedly include the baseline equivalent of the endpoint, clinical site, treatment, time and the treatment by time interaction. Covariates for the continuous efficacy endpoints measured at a single time point include the baseline equivalent of the endpoint, clinical site, and treatment. Covariates for the dichotomous endpoints include treatment and clinical site; however, the number of covariates will depend upon the number of events. In general, 10 events per covariate are necessary for a stable logistic regression model (Peduzzi et al, 1996). If the number of events permits the inclusion of a baseline drinking covariate, the percentage of days abstinent will be used as the covariate for the percent subjects abstinent endpoint; the percentage of heavy drinking days will be used as the covariate for the percent subjects with no heavy drinking days endpoint; however, no baseline drinking covariate will be employed for the endpoint, percent subjects with a WHO decrease in alcohol consumption, as this endpoint already adjusts for baseline drinking in its calculation. If there are only 5-9 events in one of the dichotomous endpoints then a logistic regression will be performed with treatment group as the only covariate.

Clinical site is included as a covariate because it was chosen as a stratification variable to account for between site variability in outcome. Prior to conducting the logistic regression, a blinded analysis of site by treatment group by dichotomous secondary outcome will be performed to determine if every site has an outcome. Clinical sites with fewer than 3 events will be combined for the purpose of conducting the logistic regression. The baseline equivalent of the endpoint is a strong predictor of the endpoint and will generally be included as a covariate.

Additional covariates for the efficacy endpoints may include baseline characteristics with a theoretical and/or empirical basis for a relationship with a particular endpoint. Such characteristics may include, but are not limited to, drinking goal, age, and years of regular drinking (age minus age first started drinking alcohol regularly). Prior to the unblinding of the data, matrices of correlations between these baseline characteristics and each of the secondary efficacy endpoints, pooled across blinded treatment assignment, will be produced (using Pearson for continuous variables, Spearman for categorical outcomes). Selection of baseline variables to include as covariates in the models will be based on consideration of the following criteria: at least modest correlation with outcome (i.e., $r \geq 0.20$), and clinical expertise. Each endpoint may have a unique set of covariates. Care is taken to only select a limited number of covariates such that the models are not over fitted.

9.5 Handling of Missing Data

9.5.1 Missing Data for Continuous Endpoints

Drinking data is collected in the TLFB. Prior to the subject dropping out of the study, every attempt will be made to continue to collect TLFB data. However, if the subject no longer wishes to participate in the collection of the TLFB, but agrees to a shorter drinking assessment using the Brief Drinking Questionnaire (BDQ), then, answers from the BDQ will be used in conjunction with the TLFB (if some TLFB data were provided by the subject) or in lieu of the TLFB (if no data were provided by the subject) to otherwise avoid missing data for drinking endpoints. Specifically, the BDQ has two questions assessing whether the subject had any heavy drinking days or drinking days during the period covered and will be used to assess the presence of a heavy drinking day or or a drinking day, respectively, for the drinking endpoints percentage of subjects with no heavy drinking days and percentage of subjects abstinent, respectively.

The primary analysis of the primary endpoint will be performed on available data in the Full Analysis Set with no imputation for missing data. However, a sensitivity analysis will be performed on the primary endpoint using multiple imputation for missing drinking data (Jakobsen et al, 2017). Multiple imputation replaces each missing value with a set of "m" plausible values that represent the uncertainty about the right value to impute. The multiple imputation method will be performed on transformed endpoint data, if a transformation is deemed necessary. The data will be evaluated for the pattern of missingness. If the data have monotone missingness then the regression method will be used. If the data have non-monotone missingness then the Monte Carlo method will be used (Ratitch et al, 2013). The imputation model will include a limited set of variables likely to be associated with missingness on the primary endpoint, excluding treatment assignment. The variables may include but are not limited to site, time and baseline alcohol use. The "m" imputed datasets each will be analyzed using mixed effects models then SAS PROC MIANALYZE will be used to combine the parameter estimates.

No imputation will be done for analysis of secondary endpoints.

9.6 Safety Analysis

9.6.1 Adverse Events

AEs will be coded using the most recent version of the Medical Dictionary for Regulatory Activities (MedDRA) and will be grouped by system, organ, and class (SOC) and preferred term (PT) designation. The severity, frequency, and relationship of AEs to investigational product will be presented by SOC and PT groupings. Listings of each individual AE including start date, stop date, severity, relationship to IP, outcome, action taken (including any treatment administered), and duration will be provided.

Every AE will be assessed for whether or not it qualifies as an SAE. All SAEs will be categorized and listed according to the following categories: Congenital Anomaly or Birth Defect; Persistent or Significant Disability/Incapacity; Results in Death; Requires or Prolongs

Hospitalization; Other Medically Important Serious Event; or Life-Threatening. For deaths, the date and cause of death will be collected and listed. For hospitalizations, the dates of admission and release (discharge) will be collected and listed.

Each AE (based on PT) will be counted once only for a given study subject. If the same AE occurred on multiple occasions, the highest severity will be assumed. Thus, study subjects are not counted multiple times in a given numerator in the calculation of frequencies for a specific AE. C-SSRS reports of suicidality or suicidal ideation will be reported as AEs and analyzed as AEs if the investigator determines after an interview with the subject, that the responses are consistent with suicidal ideation or attempt. Tabulation of suicidal ideation by CSSRS will be presented without hypothesis testing; answers to the C-SSRS will be provided in a subject listing.

9.6.2 Clinical Laboratory and Point of Care Tests

For clinical laboratory data, descriptive statistics will be generated for all tests performed at screening and at each clinic visit. If a laboratory analysis is repeated, the last measurement performed prior to the clinic visit will be used in the summary statistics for that clinic visit. If an unscheduled clinical laboratory visit occurs prior to a scheduled visit that is missed due to dropout, then the unscheduled visit will be used in the summary statistics for the missed scheduled clinical visit. If an unscheduled clinical laboratory visit occurs between two scheduled clinical visits, then the data from the unscheduled visit will only be presented in the listings and not in summary statistics. In addition, at each post-randomization clinic visit descriptive statistics for change from baseline will be generated. Laboratory values will be plotted as mean ± standard error over time. All laboratory measurements will be presented in the listings.

Number and percentage of positive urine drug tests and pregnancy tests for screening visits and all treatment and follow-up visits will be tabulated. Results of all urine drug tests and pregnancy tests will be presented in the listings. The percentage of subjects with a positive urine drug test at any time post start of treatment will also be presented by test type and treatment group.

9.6.3 Vital Signs, Weight, and ECG

Vital signs will be presented as summary statistics and change from baseline. The percentage of ECG results considered abnormal and clinically significant will be provided. Body weight will be presented as summary statistics and change from screening. No statistical tests will be performed. Vital signs, ECG results, and weight measurements for all visits will be presented in the listings.

9.6.4 Blood Alcohol Concentration

The number and percent of subjects at any clinic visit that have a BAC > 0 will be tabulated. All BAC measurements will be presented in the listings.

9.6.5 CIWA-AR Scores

The number and percentage of subjects who reported CIWA-AR scores ≥ 10 at any time after the start of dosing will be presented. Fisher's exact test will be performed. No modeling or imputation will be performed.

9.6.6 Buss-Perry Aggression Questionnaire (BPAQ)

The short form version of the BPAQ is used in this study and is a 12-item self-report measure aggression. Each item is assessed on a 5-point Likert scale assessing the degree to which agreesion-related statements are characterisitic of the subject during the past week. The BPAQ includes four subscales: physical aggression (4 items), verbal aggression (3 items), anger (2 items), and hostility (3 items) (Diamond and Magaletta, 2006). Scores for each subscale, which are the sum of the items, will be assessed individually. There is no total score for this scale.

Because the BPAQ is a repeated continuous measure, the BPAQ subscales wil be analyzed using the mixed effects described in Section 9.4.2. Descriptive statistics will be presented for each assessment by treatment group. No imputation will be performed.

9.6.7 Simplified Nutritional Appetite Questionnaire (SNAQ)

The 8-item Council on Nutrition appetite questionnaire scale and its 4-item derivative The Simplified Nutritional Appetite Questionnaire (SNAQ) were developed to assess appetite and predict weight loss. The changes in appetite during the study will be evaluated using the clinically simpler version of the two scales, the SNAQ (Wilson 2005). The 4 item SNAQ asks: 1) My appetite is; 2) When I eat; 3: Food tastes; and 4) Normally I eat; with 5 possible responses that are scored numerically from 1 to 5. The sum of the responses is the total scale score. A SNAQ score ≤14 indicates significant risk of at least 5% weight loss within six months. The number and percentages of subjects in each group with a SNAQ score ≤14 at each visit will be summarized. Fisher's exact test will be used at each visit. No imputation for missing data will be performed. A mixed effects analysis on the continuous SNAQ score, as described in Section 9.4.2, will be used to evaluate change over time. No imputation will be performed.

9.6.8 University of Pennsylvania Smell Identification Test (UPSIT)

The UPSIT will be assessed at screening and other clinic visits throughout the study to determine if intranasal investigational products cause any changes in sensory discrimination. It consists of 4 booklets each containing 10 microencapsulated (scratch and sniff) odors. The UPSIT test has been studied in individuals with alcohol addiction and has shown that this population generally had generally lower UPSIT scores that non-drinking controls. Outcomes will be captured in Adverse Event tables.

9.7 Drug Exposure and Retention

Medication compliance, defined as the amount of investigational product taken as a proportion of the total amount prescribed per protocol, will be evaluated for the oxytocin and placebo groups based on the Subject Diary. Average IU per day of investigational product taken based on the the vial weight difference prior to and after dispensment will also be reported overall and weekly will be reported for the oxytocin and placebo groups. Exposure and compliance averages will be compared across treatment groups using t-tests at each week and overall. If the data are meaningfully skewed then the Wilcoxon rank-sum test will be used. The same test will be used for each week and overall. The research participation rate, defined as percentage of subjects with complete drinking data, will be compared between treatment groups. A Fisher's Exact test will

be used for the overall participation rate, weekly tests will not be performed. In addition, the percentage of subjects discontinuing medication or early withdrawal from the study and a listing of these reasons for discontinuation will be provided. No statistical inference will be performed for reasons of discontinuation.

9.8 Analysis of Other Services Used

Weekly days of attendance at self-help meetings or other professional service providers to help reduce/quit drinking at study week 13 will be presented as summary statistics by treatment group. All other services used data will be presented in the listings.

9.9 Concomitant Medications, Medical History, and Pregnancy Tests

Concomitant and prior medications are collected at screening and at all study weeks and will be presented in a subject listing, as will pregnancy tests. Medical History will be coded using MedDRA, summarized in a table by treatment group and will be presented in subject listings. No statistical inference will be performed.

9.10 Eligibility and Screen Failures

Screen failures will be summarized in a table and provided in subject listings. Answers to eligibility criteria will be provided in the subject listings.

9.11 Exploratory Analyses

A number of variables will be tested as potential moderators of the medication treatment effect on the PHDD primary endpoint. Weeks 3-12 will be the period of interest. The model identified in Section 9.4.1 will be amended to include the potential moderator variable and the moderator by treatment group interaction. To aid with interpretation, continuous moderator variables will be dichotomized based on clinically accepted levels available from the literature. In the event a clinically meaningful cutoff is not available, LOESS curves will be used to identify a cut point. The LOESS curve analysis will use averaged PHDD data over study weeks 3-12, treatment group and the moderator of interest. In all approaches, an appropriate cutoff will be one that ensures a sufficient sample size in all resultant subgroups. The potential moderator variables are assessed at baseline and include: sex, IDS-30 reward/relief drinking, baseline drinks per week, measures of anxiety and depression (ECR-RS anxiety-related attachment, POMS subscales of depression and anxiety, Spielberger Trait Anxiety Inventory), Barratt Impulsiveness Scale, history of alcohol withdrawal (i.e., withdrawal question on the MINI for alcohol use disorder), and alcohol-related treatment goal.

There is interest in exploring the use of a new Hyperkatifeia Scale as an efficacy endpoint and moderator of drug response. Hyperkatifeia scores are assessed at Week 1 and Week 13 (EOS Visit 9). Exploratory analyses utilizing Hyperkatifeia Scale scores will include: 1) using the total score and subscales as an endpoints to assess treatment efficacy; and 2) conducting moderator analyses using total score and the subscales. The total score and subscales are the sum of the items.

9.12 *Ad hoc* Analyses

Ad hoc analyses may be performed on the Hyperkatifeia Scale as a planned part of exploring the utility of this scale including total scores, subscales, and individual items. *Ad hoc* analyses utilizing Hyperkatifeia Scale scores may include: 1) identification of baseline subsets and relationship to alcohol-related outcomes; 2) conducting mediator analyses; 3) factor analysis to better understand the underlying dimensions of hyperkatifeia; 4) validity of the Hyperkatifeia Scale by comparing to other measures (e.g., POMS and PROMIS scales or subscale scores); and 5) and further evaluation of the scales as endpoints to assess treatment efficacy. The data from this study could be used for meta-analyses with results of other studies to expand data availability for the proposed *ad hoc* analyses.

Ad hoc analyses may also be performed on the Drinking Goal questionnaire as a predictor and moderator of alcohol-related outcomes. Cutpoints for IDS-30 reward and relief drinkers have been proposed for high and low levels of each, creating 4 categories (Votaw et al, 2022). These categories will be related to drinking outcomes if there are sufficient sample sizes within each category.

10. VALIDATION OF PROGRAMMING CODE

All SAS codes used to generate tables and listings will be validated and reviewed before being finalized. The validation process will be used to determine that the numbers are produced by a statistically valid method and that the execution of the computations is correct. Qualified personnel who have not previously been involved in the production of the original programming codes will perform the validation procedures. Methods of validation include independent programming and comparison to data listings. Tables will be reviewed for accuracy, consistency with this plan, consistency within tables, and consistency with corresponding output. Once validation is complete, a quality control reviewer will perform a final review of the documents for accuracy and consistency. Upon completion of validation and quality review procedures, all documentation will be collected and filed in the study documentation files at Fast-Track.

11.0 REFERENCES

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12.0 TABLE, LISTING, AND FIGURE SHELLS

12.1 Tables

12.1.1 Subject Disposition, Participation, Compliance

Table 1: Subject Disposition - All Consented Subjects

	Treatment Group Placebo n (%)	Oxytocin n (%)	Total n (%)	p-value[1]
Number of Subjects Consented			xxx	
Number of Subjects Screen Failed			xxx (xx.x%)	
Number of Subjects Randomized	xxx	xxx	xxx	
Number of Subjects Randomized but Did Not Take Medication	x (xx.x%)	x (xx.x%)	x (xx.x%)	
Number of Subjects Randomized and Took at Least One Dose of Study Medication (Full Analysis Set)	xx (xx.x%)	xx (xx.x%)	xxx (xx.x%)	0.xxx
Number of Completed Subjects[2]	xx (xx.x%)	xx (xx.x%)	xxx (xx.x%)	0.xxx
Number of Subjects Discontinuing Medication, Remain in Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number of Subjects Discontinuing Medication, Drop out of Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Reason for Discontinuation				
Lost to follow up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Died	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Logistical or practical reasons	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Lack of perceived efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Absent from the protocol due to confinement in a controlled environment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Subject withdrew consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Clinical deterioration	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Prefer another treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Protocol non-compliance	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other reason	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

[1] p-value from Fisher's exact test for binary [2]Subjects completing Week 13 visit by phone or clinic

Programmer Notes: The discontinuation reasons are as given on the CRF. Include only the reasons actually used for the subjects in the study. If a subject discontinued, but the specific reason is missing, include 'Missing' as a row in the table. Use the order of discontinuation reasons as presented on the CRF page

Table 2: Reasons for Screen Failure – All Consented Subjects

Category	**Reason**	n (%)
Inclusion	Too young	xxx (xx.x%)
	… Refuse to take study medication	xxx (xx.x%)
Exclusion	Current substance abuse disorder	xxx (xx.x%)
	… Other reason	xxx (xx.x%)

Programmer list all reasons identified for screen failure with denominator being all consented subjects

Table 3: Exposure to Investigational Products Based on Subject Diary

	Placebo						**Oxytocin**						
Period	**N**	**Mean**	**SD**	**Med**	**Min**	**Max**	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**p-value[1]**
Insufflations[2]													
Week 1 (xx)[3]	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 2 (xx)	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 3 (xx) … Week 12 (xx)	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Overall (Weeks 1-12)													
Total number of insufflations	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Total number of insufflations Weeks 1-2	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Total number of insufflations Weeks 3-12	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w).
[2]Number of insufflations per week
[3]xx maximum number.possibible in week

Table 4: Percent Compliance to Investigational Products Based on Subject Diary

Period	Placebo						Oxytocin						p-value[1]
	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max	
Insufflations[2]													
Week 1	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 2	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 3 … Week 12	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Overall (Weeks 1-12)													
Total number of insufflations	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Total number of insufflations Weeks 1-2	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Total number of insufflations Weeks 3-12	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w).
[2] percent is the # of sprays taken/#of sprays presecribed in a period

Table 5: Exposure to Investigational Products Based on Weight of Vials

Note that this is the same as Table 2 except using IU for dosing

Table 6: Percent Compliance to Investigational Products Based on Weight of Vials

Note that this is the same as Table 3 except using IU for dosing and percent is based upon IU taken/IU presecribed

Table 7: Summary of Medical History

MedDRA SOC/ Preferred Term	Placebo (N=xx)	Oxytocin (N=xx)
SOC	nn (xx.x%)	nn (xx.x%)
- Overall -		
Preferred term 1	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)

Table 8:` Exit Interview

Question	Placebo (N=xx)	Oxytocin (N=xx)	Total (N=xxx)	p-value[1]
What medication do you believe you were taking?				0.xxx
Placebo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Active	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Both Active & Placebo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No Idea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other substance	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	
Correctly Guessed Medication (Subjects that guessed a medication)				0.xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Why did you answer above?				0.xxx
Had side effects	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Had no side effects	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Staff treated me different	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No improvement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Had improvement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Had a hunch	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
I just felt different	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	
Do you feel the medication helped you to reduce drinking?				0.xxx
Very Much	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Much	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Moderately	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
A little	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not at all	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	

	Placebo	Oxytocin	Total	
Question	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
How would you describe your experience taking the medication?				0.xxx
Experienced no unwanted side effects and benefited	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced some unwanted side effects but benefited	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced a lot unwanted side effects but benefited	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced no unwanted side effects but did not benefit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced some unwanted side effects and did not benefit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced a lot of unwanted side effects and did not benefit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	
If a friend were in need of help for a drinking problem, would you recommend taking the medication to him/her?				0.xxx
Yes, definitely	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Yes, generally	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Neither yes nor no	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No, not really	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No, definitely not	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	Xx	xx	
If you were to need treatment in the future, would you choose to take the medication again?				0.xxx
Definitely yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Generally yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Neither yes or no	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No, not really	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Definitely not	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	Xx	xx	
How much do you think of yourself as wanting to please other people (people pleaser)?				0.xxx
More than average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Less than average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Refuse to answer	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	Xx	xx	

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical variables (c).

Table 9: Research Participation by Treatment Group and Week

	Placebo (N=xx)			Oxytocin (N=xx)			
Study Week[2]	**n**	**Cumulative n**	**Cumulative %**	**n**	**Cumulative n**	**Cumulative %**	**p-value[1]**
Week 1	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 2	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 3	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 4	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 5	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 6	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 7	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 8	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 9	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 10	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 11	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 12	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 13	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx

[1] Fisher's exact test

[2]Numbers and percentages are based on subjects that participated through a given week

Table 10: Number and Percent of Subjects with Drinking Data Provided by the Brief Drinking Questionnaire instead of the TLFB

	Placebo		Oxytocin		
Study Week	**n**	**%**	**n**	**%**	**p-value[1]**
Week 3	xx	xx.x%	xx	xx.x%	0.xxx
Week 4	xx	xx.x%	xx	xx.x%	0.xxx
Week 5	xx	xx.x%	xx	xx.x%	0.xxx
Week 6	xx	xx.x%	xx	xx.x%	0.xxx
Week 7	xx	xx.x%	xx	xx.x%	0.xxx
Week 8	xx	xx.x%	xx	xx.x%	0.xxx
Week 9	xx	xx.x%	xx	xx.x%	0.xxx
Week 10	xx	xx.x%	xx	xx.x%	0.xxx
Week 11	xx	xx.x%	xx	xx.x%	0.xxx
Week 12	xx	xx.x%	xx	xx.x%	0.xxx
Overall	xx	xx.x%	xx	xx.x%	0.xxx

[1]Fisher's exact test

Note only rows with values above 0 will be presented

Table 11: Demographic Characteristics

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Age (years)				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Gender at Birth				0.xxx
N				
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Race				0.xxx
N	xx	xx	xx	
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
African-American or Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
American Indian or Alaskan Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
More than one race or other race	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unknown or not reported	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Ethnicity				0.xxx
N	xx	xx	xx	
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not reported	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Race/Ethnicity				0.xxx
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Education (years)				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Education				0.xxx
≤ High School	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
> High School	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Marital Status				0.xxx
Legally Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Living with Partner / Cohabitating	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Widowed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Separated	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Divorced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Never Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Marital Status				0.xxx
Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Employment Pattern (last 30 days)				0.xxx
Full-time > 35 hrs /week	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Part-time regular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Part-time irregular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Student	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Military Service	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unemployed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Retired/Disabled	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Homemaker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
In controlled environment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unknown	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Employment				0.xxx
Employed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unemployed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Income				0.xxx
$0-$15,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
$15,001-$30,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
$30,001-$45,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
$45,001-60,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
$60,001-75,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
$75,001-90,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
$90,001-105,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
$105,001-120,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
>$120,000	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	
Occupation				0.xxx
Corporate Executive or Major Professional	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Business Manager or Minor Professional	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Business Administrator, Small Business Owner, or Semi-professional	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Clerical Worker, Sales, or Technician	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Skilled Worker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Semi-skilled Worker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unskilled Worker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other Occupation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unemployed (not paid for services)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Never Worked	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing/ Not Given	xx	xx	xx	

1 p-value from chi-square test (c), t-test for continuous data, and Fisher's exact test for binary categories (f)

Table 12: Baseline DSM-5 Disorders

	Placebo (N=xx)	Oxytocin (N=xx)	Total (N=xxx)
DSM-5 Disorders[1]			
Major Depressive Episode	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Major Depressive Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Suicidality	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Suicide Behavior Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Manic episode	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypomanic episode	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bipolar I Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bipolar II Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other Specified Bipolar Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Panic Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Agoraphobia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Social Anxiety Disorder (Social Phobia)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Obsessive Compulsive Disorder (Past month)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Posttraumatic Stress Disorder (Past month)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Alcohol Use Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Substance Abuse Disorder (Non-alcohol)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Any Psychotic Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mood Disorder with Psychotic Features	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Major Depressive Disorder with Psychotic Features	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bipolar I Disorder with Psychotic Features	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Anorexia Nervosa (past 3 months)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Bulemia Nervosa (past 3 months)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Binge-eating Disorder (past 3 months)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Generalized Anxiety Disorder (past 6 months)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Medical, Organic, Drug Case Ruled Out	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Antisocial Personality Disorder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] As assessed by MINI

Table 13: Baseline Drinking-related Behavior and Characteristics

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Drinking Goal (n, %)				0.xxx
Total Abstinence	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Reduce but not stop	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Goal of no Heavy Alcohol Use (n, %)[2]				0.xxx
Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	
Goal of at least 50% Reduction in Drinks Per Week[3]				
N	xx	xx	xx	0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Motivation to Reach Goal				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx – xx)	
Confidence to Reach Goal				
N	xx	xx	xx	0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx – xx)	
AUD Symptom Severity				0.xxx
Moderate (4 or 5 symptoms)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Severe (6 or more symptoms)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
AUD Number of Symptoms				0.xxx
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
7	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
8	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
9	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
10	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
11	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
AUD Number of Symptoms (continuous)				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Age when first started drinking				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Number Lifetime Hospitalizations to Reduce/Quit Drinking				
N	xx	xx	xx	0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Number Lifetime Hospitalizations for Illness/ Injuries due to Drinking				
N	xx	xx	xx	0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Number Outpatient Visits to Reduce/Quit Drinking in Last 12 Months				
N	xx	xx	xx	0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Number Lifetime Medical Detoxifications				
N	xx	xx	xx	0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Past Year Number of Support Group Meetings[4]				
N	xx	xx	xx	0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	

Note: Percentages are based on the number of non-missing values in each variable.
[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical variables (c) – Fisher's exact test for dichotomous variables (f)
[2] No HDD and <=14 drinks per week for men or <=7 drinks per week women
[3] Calculated using the subject's drinks per week during 28-day pre-screen period and the drinks per week obtained from the 7-day period on the Drinking Goal assessment
[4] Examples include Alcoholics Anonymous (AA), 12 step, Save Ourselves, or similar group meetings attended for alcohol problems or drinking

Table 14: Baseline Drinking by TLFB

	Placebo	Oxytocin	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Percentage of Heavy Drinking Days (Pre-screening Days -1 to -28)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Percentage of Heavy Drinking Days (7 Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Percentage of Heavy Drinking Days (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	

	Placebo	Oxytocin	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Drinks/Week (Pre-screening Days -1 to -28)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Drinks/Week (7 Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Drinks/Week (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Drinks/Drinking Day (Pre-screening Days -1 to -28)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Drinks/Drinking Day (7Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Drinks/Drinking Day (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Percentage Days Abstinent (Pre-screening Days -1 to -28)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	

	Placebo	Oxytocin	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Percentage Days Abstinent (7 Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Percentage Days Abstinent (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx_	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
WHO Risk Level				0.xxx
High Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Very High Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Note: Percentages are based on the number of non-missing values in each variable.
[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical variables (c)

Table 15: Baseline Other Substance Use

	Placebo	Oxytocin	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Cigarette Smoker?				0.xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Any Nicotine Use?				0.xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Any Other Nicotine Product Use?				0.xxx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
THC				0.xxx
Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

	Placebo	Oxytocin	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Cigarette Smoker?				0.xxx
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Note: Percentages are based on the number of non-missing values in each variable. [1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical (c), Fisher's exact test for binary variables (f)
Programmer's note: Place the parenthesis and character after each p-value to denote the test

Table 16: Baseline POMS

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Tension-Anxiety				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Depression-Dejection				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Anger-Hostility				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Fatigue-Inertia				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	

	Placebo	Oxytocin	Total	
Characteristic	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Confusion-Bewilderment				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Vigor-Activity				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Total Mood Disturbance				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

Note: 1 p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w)

Table 17: Baseline Alcohol-Related Craving, Consequences, and Withdrawal

	Placebo	Oxytocin	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
IDS Reward Drinking Score				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Scale Min-Max			(xx.x – xx.x)	

	Placebo	Oxytocin	Total	
Parameter	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
IDS Relief Drinker Score				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Scale Min-Max			(xx.x – xx.x)	
IDS Reward Drinker N (%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
CIWA-AR				0.xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
Median	xx.x	xx.x	xx.x	
(Min – Max)	(xx.x – xx.x)	(xx.x – xx.x)	(xx.x – xx.x)	
Scale Min-Max			(xx.x – xx.x)	
No. Subjects with Withdrawal Symptoms (CIWA ≥ 10)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx

Note: 1 p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w); chi-squared test for symptoms (c)

Programmer's note: Place the parenthesis and character after each p-value to denote the test

Table 18: Baseline Mood Questionnaires

	Placebo	Oxytocin	Total	
Scale	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
BIS Brief				
Total Score				
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
STAI (T-Anxiety Scale)				0.xxx
N	xx	xx	xx	

	Placebo	Oxytocin	Total	
Scale	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
BPAQ				
Physical Aggression				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Anger				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Verbal Aggression				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Hostility				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

. [1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w)

Table 19: Baseline ECR-RS

	Placebo	Oxytocin	Total	
Subscale	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Attachment-related				
Anxiety				0.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w)

Table 20: Baseline SNAQ

	Placebo	Oxytocin	Total	
SNAQ	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Total Score				0.xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median	xxx.xx	xxx.xx	xxx.xx	
(Min – Max)	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Dichotomized				0.xxx
15+	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
≤14	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) Fisher's exact test for binary variables (f)

Table 21: Baseline PROMIS Subscales

	Placebo	Oxytocin	Total	
Subscale	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Alcohol Use Negative Consequences				0.xxx
N	xx	xx	xx	
Mean (SD_	xx.x (xx.xx)	xx.x (xx.xx)	xx.x(xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Sleep Disturbances				0.xxx
N	xx	xx	xx	
Mean (SD_	xx.x (xx.xx)	xx.x (xx.xx)	xx.x(xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Pain Interference				0.xxx
N	xx	xx	xx	
Mean (SD_	xx.x (xx.xx)	xx.x (xx.xx)	xx.x(xx.xx)	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w)

Table 22: Baseline UPSIT

	Placebo	Oxytocin	Total	
UPSIT	**(N=xx)**	**(N=xx)**	**(N=xxx)**	**p-value[1]**
Categories				0.xxx
Normosmia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Mild microsmia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Moderate microsmia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Severe microsmia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Anosmia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w)

12.1.2 Primary Efficacy Endpoint

Table 23: Weekly Percentage of Heavy Drinking Days from Baseline to Week 12

	Oxytocin				Placebo				
Study Week	**N**	**Mean (SD)**	**Median**	**Min - Max**	**N**	**Mean (SD)**	**Median**	**Min - Max**	**p-value[1]**
Baseline	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
1	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
2	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
3	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
4	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
5	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
6	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
7	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
8	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
9	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
10	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
11	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
12	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
3-12	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	

[1]t-tests for each individual week. Week 3-12 is evaluated in modeling

{programmer note: change test to Wilcoxon if the data are skewed}

Table 24: Percentage of Heavy Drinking Days per Week –Mixed Effects , Weeks 3-12, No Imputation

Type III Wald Tests[1]

Parameter	**Num DF**	**Den DF**	**F Value**	**p-value**
ARM	1	xxx	xxx.xx	0.xxx
Week	10	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	9	xxx	xxx.xx	0.xxx

[1]Values in Type III table are based upon transformed data {note to specify which transformation}

Least Squares Means[1]

				95% CI				Untransformed		Transformed	
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Oxytocin	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	11	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

[1]Values are based on untransformed data unless otherwise specified

Table 25: Percentage of Heavy Drinking Days per Week – Multiple Imputation for Missing Values, Mixed Effects, Weeks 3-12

Least Squares Means

				95% CI				Untransformed	
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**
Oxytocin	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	11	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx				
Oxytocin	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx				

12.1.3 Secondary Efficacy Endpoints

Table 26: Drinks per Week from Baseline to Week 12

	Oxytocin				Placebo				
Study Week	**N**	**Mean (SD)**	**Median**	**Min - Max**	**N**	**Mean (SD)**	**Median**	**Min - Max**	**p-value[1]**
Baseline	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
1	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
2	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
3	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
4	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
5	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
6	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
7	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
8	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
9	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
10	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
11	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
12	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	xxx
3-12	xx	xxx (xx.xx)	xxx	xxx - xxx	xxx	xxx (xx.xx)	xxx	xxx - xxx	

[1]t-tests for each individual week. Week 3-12 is evaluated in modeling

{programmer note: change test to Wilcoxon if the data are skewed}

Table 27: Drinks per Week – Mixed Effects, Weeks 3-12

Type III Wald Tests[1]

Parameter	**Num DF**	**Den DF**	**F Value**	**p-value**
ARM	1	xxx	xxx.xx	0.xxx
Week	10	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	9	xxx	xxx.xx	0.xxx

[1]Values in Type III table are based upon transformed data {note to specify which transformation}

Least Squares Means[1]

				95% CI				Untransformed		Transformed	
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Oxytocin	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	11	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx						

				95% CI				Untransformed		Transformed	
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Oxytocin	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

[1]Values are based on untransformed data unless otherwise specified

Table 28: Drinks per Drinking Day from Baseline to Week 12

Same format as Table 18

Table 29: Drinks per Drinking Day – Mixed Effects, Weeks 3-12

Same format as Table 19

Table 30: Percent Days Abstinent from Baseline to Week 12

Same format as Table 18

Table 31: Percent Days Abstinent – Mixed Effects, Weeks 3-12

Same format as Table 19

Table 32: WHO Shift Baseline to Weeks 3-12

Baseline Category	Week 3-12 Category[a]				
	Abstinent n (%)	Low Risk n (%)	Medium Risk n (%)	High Risk n (%)	Very High Risk n (%)
High Risk					
Very High Risk					

[a] Percent is based upon row denominator (eg # subjects with High Risk at baseline)

Same table for Oxytocin subjects only

Same table for Placebo subjects only

Table 33: WHO 1-Level Decrease in Alcohol Consumption – Weeks 3-12

	Placebo	**Oxytocin**	**Total**
	(N=xx)	**(N=xx)**	**(N=xxx)**
WHO 1-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 34: WHO 1-Level Decrease in Alcohol Consumption – Full Model, Logistic Regression, Weeks 3-12

								95% CI	
Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**OR**	**Upper CI**	**Lower CI**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx			
Treatment	Oxytocin	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx			
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

Table 35: WHO 1-Level Decrease in Alcohol Consumption – Weeks 9-12 (2 Month Grace)

Same style as Table 33

Table 36: WHO 1-Level Decrease in Alcohol Consumption – Full Model, Logistic Regression, Weeks 9-12 (2 Month Grace)

Same style as Table 34

Table 37: WHO 1-Level Decrease in Alcohol Consumption – Weeks 5-12 (1 Month Grace)

Same style as Table 33

Table 38: WHO 1-Level Decrease in Alcohol Consumption – Full Model, Logistic Regression, Weeks 5-12 (1 Month Grace)

Same style as Table 34

Table 39: WHO 1-Level Decrease in Alcohol Consumption Monthly

	Placebo (N=xx)	Oxytocin (N=xx)	Total (N=xxx)
Mo 2 WHO 1-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mo 3 WHO 1-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 40: Monthly Summary of WHO 1-Level Decrease in Alcohol Consumption – Full Model

									95% CI	
Model Month[a]	**Parameter**		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**OR**	**Upper CI**	**Lower CI**
2	Treatment	Oxytocin	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
3	Treatment	Oxytocin	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

Adjusted Prevalence Estimates[1]

					OR 95% CI		
Arm	**Month**	**Estimate**	**SE**	**OR**	**Lower CI**	**Upper CI**	**p-value**
Oxytocin	2	xx.xx	0.xxx	0.xxx	x.xxx	0.xxx	xx.xxx
Placebo	2	xx.xx	0.xxx	0.xxx			
Oxytocin	3	xx.xx	0.xxx	0.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx			

[1]The adjusted prevalence rates are obtained from the monthly logistic regression models

Table 41: WHO 2-Level Decrease in Alcohol Consumption – Weeks 3-12

Same as Table 33

Table 42: WHO 2-Level Decrease in Alcohol Consumption – Full Model, Logistic Regression, Weeks 3-12

Same as Table 34

Table 43: WHO 2-Level Decrease in Alcohol Consumption – Weeks 9-12 (2 Month Grace)

Same style as Table 33

Table 44: WHO 2-Level Decrease in Alcohol Consumption – Full Model, Logistic Regression, Weeks 9-12 (2 Month Grace)

Same style as Table 34

Table 45: WHO 2-Level Decrease in Alcohol Consumption – Weeks 5-12 (1 Month Grace)

Same style as Table 33

Table 46: WHO 2-Level Decrease in Alcohol Consumption – Full Model, Logistic Regression, Weeks 5-12 (1 Month Grace)

Same style as Table 34

Table 47: WHO 2-Level Decrease in Alcohol Consumption Monthly

Same style as Table 39

Table 48: Monthly Summary of WHO 2-Level Decrease in Alcohol Consumption – Full Model

Same style as Table 40

Table 49: Subjects Abstinent from Alcohol – Weeks 3-12

	Placebo	**Oxytocin**	**Total**
	(N=xx)	**(N=xx)**	**(N=xxx)**
Completely Abstinent			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 50: Subjects Abstinent from Alcohol – Full Model, Logistic Regression, Weeks 3-12

								95% CI	
Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**OR**	**Upper CI**	**Lower CI**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx			
Treatment	Oxytocin	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx			
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

Table 51: Subjects Abstinent from Alcohol – Weeks 9-12 (2 Month Grace)

Same as Table 49

Table 52: Subjects Abstinent from Alcohol – Full Model, Logistic Regression, Weeks 9-12 (2 Month Grace)

Same as Table 50

Table 53: Subjects Abstinent from Alcohol – Weeks 5-12 (1 Month Grace)

Same as Table 49

Table 54: Subjects Abstinent from Alcohol – Full Model, Logistic Regression, Weeks 5-12 (1 Month Grace)

Same as Table 50

Table 55: Subjects Abstinent from Alcohol Monthly

	Placebo	**Oxytocin**	**Total**
	(N=xx)	**(N=xx)**	**(N=xxx)**
Mo 2 Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mo 3 Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 56: Monthly Summary of Subjects Abstinent from Alcohol – Full Model

									95% CI	
Model Month[a]	**Parameter**		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**OR**	**Upper CI**	**Lower CI**
2	Treatment	Oxytocin	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
3	Treatment	Oxytocin	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

[a] Separate models are created for each month; only the treatment arm results are presented in the summary table

Adjusted Prevalence Estimates[1]

					OR 95% CI		
Arm	**Month**	**Estimate**	**SE**	**OR**	**Lower CI**	**Upper CI**	**p-value**
Oxytocin	2	xx.xx	0.xxx	0.xxx	x.xxx	0.xxx	xx.xxx
Placebo	2	xx.xx	0.xxx	0.xxx			
Oxytocin	3	xx.xx	0.xxx	0.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx			

[1]The adjusted prevalence rates are obtained from the monthly logistic regression models

Table 57: Subjects No Heavy Drinking Days – Weeks 3-12

	Placebo	**Oxytocin**	**Total**
	(N=xx)	**(N=xx)**	**(N=xxx)**
No Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 58: Subjects No Heavy Drinking Days – Full Model, Logistic Regression, Weeks 3-12

Same as Table 50

Table 59: Subjects No Heavy Drinking Days – Weeks 9-12 (2 Month Grace)

Same as Table 49

Table 60: Subjects No Heavy Drinking Days – Full Model, Logistic Regression, Weeks 9-12 (2 Month Grace)

Sam as Table 50

Table 61: Subjects No Heavy Drinking Days – Weeks 5-12 (1 Month Grace)

Same as Table 49

Table 62: Subjects No Heavy Drinking Days – Full Model, Logistic Regression, Weeks 5-12 (1 Month Grace)

Same as Table 50

Table 63: Subjects No Heavy Drinking Days -- Monthly

Same style as Table 55

Table 64: Monthly Summary of Subjects No Heavy Drinking Days – Full Model

Same style as Table 56

Table 65: Urge to Drink Scale – Each Evaluation During Maintenance Period

	Oxytocin						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 66: Urge to Drink Scale – Full Model, Mixed Effects, Weeks 6-13

Type III Wald Tests[1]

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	X	xxx	xxx.xx	0.xxx
ARM*Week	3	xxx	xxx.xx	0.xxx

[1]Values in Type III table are based upon transformed data {note to specify which transformation}

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Oxytocin	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	13	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	13	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 67: ECR-RS (attachment related anxiety) – Each Evaluation During Maintenance Period

	Oxytocin						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Anxiety												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 68: ECR-RS Attachment-Related Anxiety – Full Model, Mixed Effects, Weeks 6-13

Same as Table 66

Table 69: POMS – Each Evaluation During Maintenance Period

	Oxytocin						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Tension-Anxiety												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Depression-Dejection												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Anger-Hostility												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Vigor-Activity												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Fatigue-Inertia												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Confusion-Bewilderment												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Total Mood Disturbance												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 70: POMS Tension-Anxiety – Full Model, Mixed Effects, Weeks 6-13

Shell is the same style as Table 66

Table 71: POMS Depression-Dejection – Full Model, Mixed Effects, Weeks 6-13

Shell is same style as Table 66

Table 72: POMS Anger-Hostility – Full Model, Mixed Effects, Weeks 6-13

Shell is same style as Table 66

Table 73: POMS Vigor-Activity – Full Model, Mixed Effects, Weeks 6-13

Shell is same style as Table 66

Table 74: POMS Fatigue-Inertia – Full Model, Mixed Effects, Weeks 6-13

Shell is same style as Table 66

Table 75: POMS Confusion-Bewilderment – Full Model, Mixed Effects, Weeks 6-13

Shell is same style as Table 66

Table 76: POMS Total Mood Disturbance – Full Model, Mixed Effects, Weeks 6-13

Shell is same style as Table 66

Table 77: PROMIS – Each Evaluation During Maintenance Period

	Oxytocin						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Alcohol Negative Consequences												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Sleep Disturbances												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Pain Interference												
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 78: PROMIS Alcohol Use Negative Consequences – Full Model, Mixed Effects, Weeks 6-13

Shell is the same style as Table 66

Table 79: PROMIS Sleep Disturbances – Full Model, Mixed Effects, Weeks 6-13

Shell is the same style as Table 66

Table 80: PROMIS Pain Interference – Full Model, Mixed Effects, Weeks 6-13

Shell is the same style as Table 66

Table 81: Mean Cigarettes Smoked per Week (among smokers) – Each Evaluation During Maintenance Period

	Oxytocin						**Placebo**					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 82: Mean Cigarettes Smoked per Week (among Smokers) – Full Model, Mixed Effects, Weeks 6-13

Same as Table 66

Table 83: Mean Days Use of Other Nicotine Products – Each Evaluation During Maintenance Period

Same as Table 81

Table 84: Mean Use of Other Nicotine Products – Full Model, Mixed Effects, Weeks 6-13

Same as Table 66

Table 85: Subjects Abstinent from Cigarettes among Smokers Weeks 6-13

	Placebo	**Oxytocin**	**Total**
	(N=xx)	**(N=xx)**	**(N=xxx)**
Completely Abstinent			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 86: Subjects Abstinent from Cigarettes (among Smokers) – Logistic Regression, Weeks 6-13

								95% CI	
Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**OR**	**Upper CI**	**Lower CI**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx			
Treatment	Oxytocin	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx			
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx			
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

Table 87: MINI AUD Number of Symptoms

	Oxytocin						**Placebo**					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 88: MINI AUD Number of Symptoms – Analysis of Covariance, Week 13

Type III Wald Tests

Parameter	**Num DF**	**Den DF**	**F Value**	**p-value**
ARM	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
MINI AUD	1	xxx	xxx.xx	0.xxx

Least Squares Means

			95% CI				Untransformed		Transformed	
Arm	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Oxytocin	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx						

12.1.4 Safety Analyses

Table 89: Overall Summary of Adverse Events

	Placebo	Oxytocin	Total	
	(N=xx)	(N=xx)	(N=xxx)	p-value[1]
Number of AEs	xx	xx	xx	
Number of SAEs	xx	xx	xx	
Number (%) of subjects with at least one AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number (%) of subjects with at least one SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number (%) of subjects with at least one AE related[2] to study product	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number of AEs by severity				
Mild	xx	xx	xx	
Moderate	xx	xx	xx	
Severe	xx	xx	xx	
Life-threatening	xx	xx	xx	
Number of AEs by relationship to study product				
At least possibly related	xx	xx	xx	
Unrelated	xx	xx	xx	
Number of AEs by SAE status				
No	xx	xx	xx	
Yes	xx	xx	xx	

[1]p-value from chi-square test [2] Related is possible, probable, or definite

Table 90: Number and Percentage of Subjects with Adverse Events

MedDRA System Organ Class/	**Placebo**	**Oxytocin**	**p-value[1]**
Preferred Term	**(N=xx)**	**(N=xx)**	
- Any Adverse Events -	xx (xx.x%)	xx (xx.x%)	0.xxx
SOC			
- Overall -	xx (xx.x%)	xx (xx.x%)	0.xxx
Preferred term 1	xx (xx.x%)	xx (xx.x%)	
Preferred term 2	xx (xx.x%)	xx (xx.x%)	

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
[1] Fisher's exact test
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 91: Number and Percentage of Subjects with Adverse Events During Weeks 1 & 2

Same as Table 90 except only the first 2 weeks

Table 92: Number and Percentage of Subjects with Adverse Events During Weeks 3-12

Same as Table 90 except only the last 10 weeks

Table 93: Summary of Subjects with Adverse Events by Severity and Relationship – Oxytocin

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 94: Summary of Subjects with Adverse Events by Severity and Relationship – Placebo

Number of Subjects (%) (N=x)												
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 95: Number and Percentage of Subjects with Adverse Events by Maximum Severity

MedDRA SOC/	**Placebo**				**Oxytocin**			
Preferred Term	**(N=xx)**				**(N=xx)**			
	Mild	**Moderate**	**Severe**	**Life-threatening**	**Mild**	**Moderate**	**Severe**	**Life-threatening**
- Any Adverse Events -	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
SOC								
- Overall -	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 1	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 96: Number and Percentage of Subjects with Adverse Events by Maximum Severity During Weeks 1& 2

Same as Table 95 using only first 2 weeks

Table 97: Number and Percentage of Subjects with Adverse Events by Maximum Severity During Weeks 3-12

Same as Table 95 using only weeks 3-12

Table 98: Number and Percentage of Subjects with Adverse Events Occurring in >= 5%

MedDRA SOC/ Preferred Term	Placebo (N=xx)	Oxytocin (N=xx)	p-value[1]
SOC	nn (xx.x%)	nn (xx.x%)	0.xxx
- Overall -			
Preferred term 1	nn (xx.x%)	nn (xx.x%)	0.xxx
Preferred term 2	nn (xx.x%)	nn (xx.x%)	0.xxx

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term. At least 5% occurring in either arm to be included in the table.
1 Fisher's Exact test
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 99: Number and Percentage of Subjects with Adverse Events Leading to Discontinuation of Study

MedDRA SOC/ Preferred Term	Placebo (N=xx)	Oxytocin (N=xx)
SOC	nn (xx.x%)	nn (xx.x%)
- Overall -		
Preferred term 1	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 100: Number and Percentage of Subjects with Adverse Events Leading to Discontinuation of Study Medication

MedDRA SOC/ Preferred Term	Placebo (N=xx)	Oxytocin (N=xx)
SOC	nn (xx.x%)	nn (xx.x%)
- Overall -		
Preferred term 1	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 101: CIWA-AR Score $\geq$ 10 at Least Once During Treatment

							95% CI	
	Placebo	Oxytocin	Total					
	(N=xx)	(N=xx)	(N=xxx)	p-value[1]	Cohen's h	Odds Ratio	OR Lower CI	OR Upper CI
CIWA-AR Score >= 10								
Never	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)					
At Least Once	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx	0.xx	xx.xxx	xx.xxx	xx.xxx

1 Chi-squared test

Table 102: Summary of Vital Signs and Body Weights

Parameter	N	Mean	SD	Med	Max	Min
Vital Sign (units)						
Screening						
Placebo	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Oxytocin	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Week 1						
Placebo	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Oxytocin	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Change from baseline						
Placebo	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Oxytocin	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Weeks 1, 2, 3, 4, 6, 8, 10, 13						

Programmers note: vital signs include pulse rate, systolic blood pressure, and diastolic blood pressure. Body weight (lbs) will also be presented for screening, Weeks 6, 8, 10 and 13.

Table 103: Incidence of Abnormal Findings on Physical Exam in Nasal Mucosa

	Placebo	Oxytocin
	(N=xx)	**(N=xx)**
Abnomal Nasal Mucosa	nn (xx.x%)	nn (xx.x%)

Table 104: Summary of Other Services Used During Treatment Period

	Placebo	Oxytocin
Services	**(N=xx)**	**(N=xx)**
Self Help Meetings		
N	xx	xx
Mean	xx.x	xx.x
SD	xxx.xx	xxx.xx
Median	xx	xx
Min-Max	(xx-xx)	(xx-xx)

	Placebo	Oxytocin
Services	**(N=xx)**	**(N=xx)**
Have you visited another health professional to get help reducing drinking?		
N	Xx	xx
Yes n (%)	xx (xx)	xx (xx)

Programmer note: categorize type of professional for those categories reaching 5%

Table 105: Summary of ECG Results

	ASP8062	Placebo
Result	**(N=xx)**	**(N=xx)**
Screening		
Normal	nn (xx.x%)	nn (xx.x%)
Abnormal, Not Clinically Significant	nn (xx.x%)	nn (xx.x%)
Abnormal, Clinically Significant	nn (xx.x%)	nn (xx.x%)
End of Study		
Normal	nn (xx.x%)	nn (xx.x%)
Abnormal, Not Clinically Significant	nn (xx.x%)	nn (xx.x%)
Abnormal, Clinically Significant	nn (xx.x%)	nn (xx.x%)

Table 106: Summary of Blood Chemistries

	Placebo						Oxytocin					
Test	**N**	**Mean**	**SD**	**Med**	**Min**	**Max**	**N**	**Mean**	**SD**	**Med**	**Min**	**Max**
Test Name (units)												
Screening												
Week 6												
Change from baseline												
Weeks 8, 10, 13												

Programmers note: table will include creatinine, ALT, AST, total bilirubin, creatinine, sodium, and potassium.

Table 107: Summary of Positive Urine Drug Tests, Pregnancy Test or BAC > 0.000 Any Time During the Study

	Number (% Positive)	
Test	**Placebo**	**Oxytocin**
THC	xx (xx%)	xx (xx%)
Cocaine	xx (xx%)	xx (xx%)
Opioids	xx (xx%)	xx (xx%)
Methamphetamine	xx (xx%)	xx (xx%)
Amphetamine	xx (xx%)	xx (xx%)
Benzodiazapines	xx (xx%)	xx (xx%)
Buprenorphine	xx (xx%)	xx (xx%)
Methadone	xx (xx%)	xx (xx%)
Oxycodone	xx (xx%)	xx (xx%)
MDMA	xx (xx%)	xx (xx%)
Barbiturates	xx (xx%)	xx (xx%)
Pregnancy	xx (xx%)	xx (xx%)
BAC > 0.000	xx (xx%)	xx (xx%)

Table 108: BPAQ – Each Evaluation During Maintenance Period

	Oxytocin						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Physical Aggression												
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Verbal Aggression												

6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Hostility												
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Anger												
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 109: BPAQ Physical Aggression Score -- Full Model, Mixed Effects, Entire Maintenance Period

Type III Wald Tests[1]

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Baseline Total Score	x	xxx	xxx.xx	0.xxx
ARM*Week	3	xxx	xxx.xx	0.xxx

[1]Values in Type III table are based upon transformed data {note to specify which transformation}

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Oxytocin	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	13	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	13	xx.xx	0.xxx	0.xxx	0.xxx						
Oxytocin	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 110: BPAQ Verbal Aggression Score -- Full Model, Mixed Effects, Entire Maintenance Period

Shell is same style as Table 109

Table 111: BPAQ Anger Score -- Full Model, Mixed Effects, Entire Maintenance Period

Shell is same style as Table 109

Table 112: BPAQ Hostility Score -- Full Model, Mixed Effects, Entire Maintenance Period

Shell is same style as Table 109

Table 113: SNAQ – Untransformed, Each Evaluation During Maintenance Period

	Oxytocin						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 114: SNAQ Score ≤ 14 at Each Visit During Treatment

							95% CI	
	Placebo	**Oxytocin**	**Total**					
	(N=xx)	**(N=xx)**	**(N=xxx)**	**p-value[1]**	**Cohen's h**	**Odds Ratio**	**OR Lower CI**	**OR Upper CI**
SNAQ Score ≤ 14								
Week 6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx	0.xx	xx.xxx	xx.xxx	xx.xxx
Week 8	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx	0.xx	xx.xxx	xx.xxx	xx.xxx
Week 10	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx	0.xx	xx.xxx	xx.xxx	xx.xxx
Week 13	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx	0.xx	xx.xxx	xx.xxx	xx.xxx

1 Chi-squared test

Table 115: SNAQ Total Score -- Full Model, Mixed Effects, Entire Maintenance Period

Shell is same style as Table 109

Table 116: Frequency of Subjects with Suicidal Ideation Any Time During the Study

Number of Subjects Reporting Suicidal Ideation by C-SSRS (%)		
Placebo	**Oxytocin**	**p-value**
(N=xx)	**(N=xx)**	
xx (xx.x%)	xx (xx.x%)	0.xxx

12.1.5 Exploratory Analyses

Table 117: Moderator: MINI AUD (Percent Heavy Drinking Days Weeks 3-12)

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	11	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Baseline MINI AUD	1	xxx	xxx.xx	0.xxx
ARM*MINI AUD	1	xxx	xxx.xx	0.xxx

Least Squares Means

					95% CI					
AUD Split	**Arm**	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**
Yes	Oxytocin	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
	Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx				
No	Oxytocin	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
	Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx				

Table 118: Moderator: POMS Tension-Anxiety (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 119: Moderator: POMS Depression-Dejection (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 120: Moderator: ECR-RS Attachment-Related Anxiety (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 121: Moderator: STAI (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 122: Moderator: Drinking Goal (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 123: Moderator: BIS Self Control (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 124: Moderator: BIS Impulsive Behavior (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 125: Moderator: Hyperkatifeia (Percent Heavy Drinking Days Weeks 3-12)

Shell style similar to Table 117

Table 126: Hyperkatifeia Total Score

	Oxytocin						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
Baseline	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 127: Hyperkatifeia Total Score– Generalized Linear Model, Week 13

Type III Wald Tests

Parameter	**Num DF**	**Den DF**	**F Value**	**p-value**
ARM	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Hyperkatifeia	1	xxx	xxx.xx	0.xxx

Least Squares Means

			95% CI				Untransformed		Transformed	
Arm	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Oxytocin	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx						

Table 128: Hyperkatifeia Stress/Anxiety Score

Same as Table 126

Table 129: Hyperkatifeia Stress/Anxiety Score– Generalized Linear Model, Week 13

Same as Table 127

Table 130: Hyperkatifeia Depression Score

Same as Table 126

Table 131: Hyperkatifeia Depression Score– Generalized Linear Model, Week 13

Same as Table 127

Table 132: Hyperkatifeia Irritable Score

Same as Table 126

Table 133: Hyperkatifeia Irritable Score– Generalized Linear Model, Week 13

Same as Table 127

Table 134: Hyperkatifeia Pain Score

Same as Table 126

Table 135: Hyperkatifeia Pain Score– Generalized Linear Model, Week 13

Same as Table 126

12.2 Listings

Listing 1: Subject Disposition - All Subjects

Subject ID	Date of Consent	Treatment Group	Full Analysis Set	Study Completion	(Day) Date of Study Completion or Early Discontinuation	Reason for Early Discontinuation	Subject confined or incar-cerated	Start Date/ End Date of confinement
xxx	mm/dd/yyyy	Oxytocin	Yes	Yes	(xx) mm/dd/yyyy	xxxxxx	Yes	mm/dd/yyyy / mm/dd/yyyy
		Placebo	No	No			No	
		None						

Note: Day is relative to Study Day 0.

Listing 2: Enrollment and Randomization – All Consented Subjects

Subject ID	**Treatment Group**	**Date of Consent**	**Did the subject meet all eligibility criteria?**	**Randomized?**	**Date of Randomization**	**Kit Number**
xxx	Oxytocin	mm/dd/yyyy	Yes	Yes	mm/dd/yyyy	xxx
	Placebo		No	No		

Listing 3: Reason not Eligible – Screen Failures

Subject ID	**Criterion Type**	**Criterion**
xxx	Inclusion Criteria	
	Exclusion Criteria	

Listing 4: Protocol Deviations

Subject ID	**Treatment Group**	**Deviation Date**	**Protocol Deviation**	**Details**
xxx	Oxytocin	mm/dd/yyyy	Subject Failed to Meet the Inclusion/Exclusion Criteria	
	Placebo		Source Documentation was Not Available	
			Pregnancy Test Not Performed	
			Required study data was not obtained or obtained late due to site error	
			Informed Consent Deviation	
			AE/SAE Reporting Deviation	
			Other Deviation:	xxxxxxxxxxxxxx

Note: Only subjects with protocol deviation are listed.

Listing 5: Subjects Excluded from the Efficacy Analysis

Subject ID	**Treatment Group**	**Reason for Exclusion from FA**
Xxx	Oxytocin	xxxxxx
	Placebo	

Note: Only subjects excluded from the efficacy analysis are listed.

Listing 6: Demographics Data

Subject ID	**Treatment Group**	**Gender**	**Age (yrs)**	**Ethnicity**	**Race**	**Marital Status**
xxx	Oxytocin	Male	xx	Hispanic or Latino	American Indian or Alaska Native	Married
	Placebo	Female		Not Hispanic or Latino	Asian	Divorced
				Unknown	Native Hawaiian or Other Pacific Islander	Living with Partner
					Black or African American	Widowed
					White	Separated
					Other	Never Married
					Unknown	Unknown
						Missing

Subject ID	**Treatment Group**	**Years of Education**	**Years of Formal Education (GED=12years)**	**Usual Employment Pattern in the last 30 days**
xxx	Oxytocin	xx	xxx	Full-time, 35+ hrs/week
	Placebo			Part-time, regular hours
				Part-time, irregular hours/daywork
				Student
				Military service
				Unemployed
				Retired/Disabled
				Homemaker
				In controlled environment
				Unknown

Listing 7: Baseline Drinking Characteristics

Subject ID	**Treatment Group**	**Drinks/Week (Days -1 to -28)**	**Drinks/Week (Days -1 to -7 Pre-randomization)**	**% Change Drinks per Week Pre-screen to Pre-randomization**	**Drinks/ Drinking Day (Days -1 to -28)**	**Drinks/Drinking Day (Days -1 to -7 Pre-randomization)**	**% Change DPDD Pre-screen to Pre-randomization**
xxx	Oxytocin	xxx.x	xxx.x	xx.x	xxx.x	xxx.x	xx.x
	Placebo						

Subject ID	**Treatment Group**	**Weekly % Heavy Drinking Days (Days -1 to -28)**	**Weekly % Days Abstinent (Days -1 to -28)**	**WHO Risk Level**
xxx	Oxytocin	xxx.x	xxx.x	High Risk
	Placebo			Very High Risk

Listing 8: MINI DSM5 Disorders

Subject ID	**Treatment Group**	**Visit Date**	**Diagnosis**	**Timeframe**
xxx	Oxytocin	mm/dd/yyyy	xxxxxx	Current (2 weeks)
	Placebo			Past
				Recurrent

Note: Only subjects with a diagnosis of a disorder will be listed.

Listing 9: MINI DSM5 AUD

Subject ID	**Treatment Group**	**Visit Date**	**# of Symptoms**
xxx	Oxytocin	mm/dd/yyyy	xx
	Placebo		

Listing 10: MINI AUD End of Study

Subject ID	**Treatment Group**	**Item**											**# of Symptoms**
		1	2	3	4	5	6	7	8	9	10	11	
xxx	Oxytocin	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	Placebo	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	
		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	

Item #	List of Items
1	a. During the times when you drank alcohol, did you end up drinking more than you planned when you started?
2	b. Did you repeatedly want to reduce or control your alcohol use? Did you try to cut down or control your alcohol use, but failed? IF YES TO EITHER, MARK YES.
3	c. On the days that you drank, did you spend substantial time obtaining alcohol, drinking, or recovering from the effects of alcohol?
4	d. Did you crave or have a strong desire or urge to use alcohol?
5	e. Did you spend less time meeting your responsibilities at work, at school, or at home, because of your repeated drinking?
6	f. If your drinking caused problems with your family or other people, did you still keep on drinking?
7	g. Were you intoxicated more than once in any situation where you or others were physically at risk, for example, driving a car, riding a motorbike, using machinery, boating, etc.?
8	h. Did you continue to use alcohol, even though it was clear that the alcohol had caused or worsened psychological or physical problems?
9	i. Did you reduce or give up important work, social or recreational activities because of your drinking?
10	j. Did you need to drink a lot more in order to get the same effect that you got when you first started drinking or did you get much less effect with continued use of the same amount?
11	K1. When you cut down on heavy or prolonged drinking did you have any of the following: [increased sweating or heart rate; hand tremor or “the shakes”; trouble sleeping; nausea or vomiting; hearing or seeing things other people could not see or hear or having sensations in your skin for no apparent reason; agitation; anxiety; seizures] (If yes to 2 or more of these, check yes for this question), OR K2. Did you drink alcohol to reduce or avoid withdrawal symptoms or to avoid being hung over? If K1 or K2 = yes, then score as yes.

Listing 11: Medical History

Subject ID No.	**Treatment Group**	**SOC**	**Specify (Preferred Term/ Verbatim Term)**	**Start Date**	**Ongoing**
xxx	Oxytocin	Blood and Lymphatic System Disorders	Xxxxxxxxxxx/ xxxxxxxx	mm/dd/yyyy	No
	Placebo	Cardiac Disorders			Yes
		Congenital, Familial and Genetic Disorders			
		Ear and Labyrinth Disorders			
		Endocrine Disorders			
		Eye Disorders			
		Gastrointestinal Disorders			
		General Disorders and Administration Site Conditions			
		Hepatobiliary Disorders			
		Immune System Disorders			
		Infections and Infestations			
		Injury, Poisoning and Procedural Complications			
		Investigations			
		Metabolism and Nutrition Disorders			
		Musculoskeletal and Connective Tissue Disorders			
		Neoplasms Benign, Malignant and Unspecified (incl Cysts and Polyps)			
		Nervous system Disorders			
		Pregnancy, Puerperium and Perinatal Conditions			
		Psychiatric Disorders			

		Renal and Urinary Disorders			
		Reproductive System and Breast Disorders			
		Respiratory, Thoracic and Mediastinal Disorders			
		Skin and Subcutaneous Tissue Disorders			
		Social Circumstances			
		Surgical and Medical Procedures			
		Vascular Disorders			
		Other:xxxxxxxxx			

Listing 12: Surgical History

Subject ID No.	**Treatment Group**	**Has the subject had any past surgeries?**	**Date of Surgery**	**Type of Surgery**
xxx	Oxytocin	Yes	mm/dd/yyyy	xxxxxxxxxxxxx
	Placebo	No		

Listing 13: Physical Exam

Subject ID No.	**Treatment Group**	**Exam Date**			**Any abnormal finding during the physical exam?**	**Describe**
xxx	Oxytocin	mm/dd/yyyy			Yes	xxxxxxxx
	Placebo				No	

Programming Note: Only report the items that are abnormal

Listing 14: Drinking Treatment History

Subject ID No.	**Treatment Group**	**Age first started drinking alcohol regularly**	**Number of lifetime inpatient visits to get help with reducing or quitting drinking**	**Number of lifetime inpatient hospitalizations for illnesses, injuries, or accidents due to drinking**	**Number of times in lifetime underwent alcohol detoxification using medication**	**Number of lifetime outpatient visits with a health professional to get help with reducing or quitting drinking**	**Number of group meetings attended for alcohol problems or drinking in the past year**
xxx	Oxytocin	xxx	xxx	xxx	xxx	xxx	xxx
	Placebo						

Listing 15: Drinking Goal

				Subjects wanting to reduce drinking, expected drinks per day						
Subject ID	**Treatment Group**	**Visit Date**	**Which treatment goal would you like to achieve by the end of the study?**	**Mon**	**Tues**	**Wed**	**Thur**	**Fri**	**Sat**	**Sun**
xxx	Oxytocin	mm/dd/yyyy	Abstinence	x	x	x	x	x	x	x
	Placebo		Reduction but not stop							

Subject ID	**Treatment Group**	**Visit Date**	**How motivated to reach your goal?**	**How confident to achieve your goal?**
xxx	Oxytocin	mm/dd/yyyy	1=Not Motivated	1=Not Confident
	Placebo		2, 3, 4, 5, 6, 7, 8, 9	2, 3, 4, 5, 6, 7, 8, 9
			10=Extremely Motivated	10=Extremely Confident
			Refuse to answer	Refuse to answer

Listing 16: Daily and Weekly Standard Drink Units (TLFB) During Treatment

Subject ID	Treatment Group	Week	D1	D2	D3	D4	D5	D6	D7	Mean drinks/day	Mean drinks/ drinking day	Heavy drinking days	% days abstinent
xxx	Oxytocin	1	xx	xx	xx	xx	xx	xx	xx	xx.xx	xx.xx	xx.xx	xx
	Placebo	2											
		3, etc											

Listing 17: Drinking Question

Subject ID	**Treatment Group**	**Date of Assessment**	**Did the subject have any drinking days since the last visit?**	**Did the subject have any heavy drinking days since the last visit?**	**Date of last visit**
xxx	Oxytocin	mm/dd/yyyy	Yes	Yes	mm/dd/yyyy
	Placebo		No	No	

Listing 18: Drinking Consequences, Craving, Appetite, and Anxiety

Subject ID	Treatment Group	Week	Urge to Drink	CIWA-AR	STAI	SNAQ	ECR-RS Attachment-Related Anxiety	BIS Total Score
xxx	Oxytocin	xx		xx	xx	xx	xx	xx
	Placebo							

Listing 19: UPSIT Scores

Subject ID	**Treatment Group**	**Week**	**Total Score**	**Category**
xxx	Oxytocin	xx	xx	Normosmia
	Placebo			Mild microsmia
				Moderate microsmia
				Severe microsmia
				Anosmia
				Normosmia

Listing 20: POMS Scores

			Scores						
Subject ID	**Treatment Group**	**Week**	**Total Mood Disturbance**	**Tension**	**Depression**	**Anger**	**Fatigue**	**Confusion**	**Vigor**
xxx	Oxytocin	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
	Placebo								

Listing 21: PROMIS Scale Scores

Subject ID	Treatment Group	Week	Sleep Disturbance	Alcohol Negative Consequences	Pain Interference
xxx	Oxytocin	xx	xx	xx	xx
	Placebo				

Listing 22: Smoking Data

Subject ID	**Treatment Group**	**Week**	**Visit Date**	**Over the past week, how many days did you smoke cigarettes?**	**On the days you smoked, how many cigarettes did you smoke on average?**	**How many days did you use other tobacco or nicotine products during the past week?**
xxx	Oxytocin	1, 6, 8, 10, 13	mm/dd/yyyy	x	xx	x
	Placebo					

Listing 23: Exit Interview

Subject ID	**Treatment Group**	**Visit Date**	**What study drug do you believe you were taking?**	**Why do you think you received that drug?**	**Do you feel the study drug helped you to reduced drinking?**	**How would you describe your experience taking the study drug?**
xxx	Oxytocin	mm/dd/yyyy	Placebo	Had side effects	Very Much	Experienced no unwanted side effects and benefited from taking the medication
	Placebo		Active medication	Had no side effects	Much	Experienced some unwanted side effects but benefited from taking the medication
			Both placebo and active	Staff told me	Moderately	Experienced a lot unwanted side effects but benefited from taking the medication
			Don't know	Staff treatment me different	A Little	Experienced no unwanted side effects but did not benefit from taking the medication
			Other substance	No improvement in drinking	Not Little	Experienced some unwanted side effects and did not benefit from taking the medication
				Had improvement in drinking	Not at all	Experienced a lot of unwanted side effects and did not benefit from taking the medication
				Had a hunch		
				I just felt different		
				Other: xxxxx		

Subject ID	**Treatment Group**	**Visit Date**	**If a friend were in need of help for a drinking problem, would you recommend taking the study drug to him/her?**	**If you were to need treatment in the future, would you choose to take the study drug again?**	**How much do you think of yourself as wanting to please other people (people pleaser)?**
xxx	Oxytocin	mm/dd/yyyy	Yes, definitely	Definitely yes	More than average
	Placebo		Yes, generally	Probably yes	Average
			Neither yes nor no	Maybe	Less than average
			No, not really	Probably not	
			No, definitely not	Definitely not	

Listing 24: Other Services Use

Subject ID	**Group**	**Date**	**Week**	**Since your last visit did you attend any AA, 12-step, SOS, or similar group meeting?**	**How many?**	**Have you visited another health professional to get help reducing drinking?**	**What type of professional?**
xxx	Oxytocin	mm/dd/yyyy	xx	Yes	xxxx	Yes	xxxxx
	Placebo			No		No	

Listing 25: Drug Exposure

Subject ID No.	**Treatment Group**	**Study Month**	**Date Start of Month**	**Date End of End of Month**	**Volume of Drug Prescribed**	**Volume of Drug Taken**	**Reason for Discontinuation**
xxx	Oxytocin	1, 2, 3	mm/dd/yyyy	mm/dd/yyyy	xx	xx	
	Placebo						

Listing 26: Adverse Events

Subject ID	**Treatment Group**	**Adverse Event (Verbatim) S: SOC P: PT Term**	**Start Date/ Day**	**Stop Date/ Day**	**Duration in Days**	**Severity**	**Relation -ship**	**Actions Taken**	**Outcome**	**Serious**
xxx	Oxytocin	Verbatim	mm/dd/yyyy	mm/dd/yyyy		1	1	1	1	Yes
	Placebo	S: xxxx	xx	xx		2	2	2	2	No
		P: xxxx				3	3	3	3	
						4	4	4	4	
							5	5	5	
								6		

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment
Outcome: 1=Resolved; 2=Recovered with sequelae; 3=Ongoing; 4=Required treatment; 5=Unknown

Programmer's Note: If "Were any AEs reported?" checkbox=No, then display "None Reported" in the Adverse Event column and SOC/PT column. If an AE started and stopped the same day, the duration is 1 day.

Listing 27: Adverse Events Leading to Subject Discontinuation from Study

Subject ID	**Treatment Group**	**Adverse Event (Verbatim) S: SOC P: PT Term**	**Start Date/ Day**	**Stop Date/ Day**	**Duration in Days**	**Severity**	**Relation -ship**	**Actions Taken**	**Outcome**	**Serious**
xxx	Oxytocin	Verbatim	mm/dd/yyyy	mm/dd/yyyy		1	1	1	1	Yes
	Placebo	S: xxxx	xx	xx		2	2	2	2	No
		P: xxxx				3	3	3	3	
						4	4	4	4	
							5	5	5	
								6		

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment
Outcome: 1=Resolved; 2=Recovered with sequelae; 3=Ongoing; 4=Required treatment; 5=Unknown

Programmer's Note: If "Were any AEs reported?" checkbox=No, then display "None Reported" in the Adverse Event column and SOC/PT column. If an AE started and stopped the same day, the duration is 1 day.

Listing 28: Adverse Events Leading to Discontinuation of Investigational Product

Subject ID	**Treatment Group**	**Adverse Event (Verbatim) S: SOC P: PT Term**	**Start Date/ Day**	**Stop Date/ Day**	**Duration in Days**	**Severity**	**Relation -ship**	**Actions Taken**	**Outcome**	**Serious**
xxx	Oxytocin	Verbatim	mm/dd/yyyy	mm/dd/yyyy		1	1	1	1	Yes
	Placebo	S: xxxx	xx	xx		2	2	2	2	No
		P: xxxx				3	3	3	3	
						4	4	4	4	
							5	5	5	
								6		

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment
Outcome: 1=Resolved; 2=Recovered with sequelae; 3=Ongoing; 4=Required treatment; 5=Unknown

Programmer's Note: If "Were any AEs reported?" checkbox=No, then display "None Reported" in the Adverse Event column and SOC/PT column. If an AE started and stopped the same day, the duration is 1 day.

Listing 29: Serious Adverse Events

Subject ID	**Treatment Group**	**SAE Verbatim S: SOC P: PT**	**Start Date/ Day**	**Stop Date/ Day**	**SAE Category**	**Severity**	**Relationship**
xxx	Oxytocin	Verbatim	mm/dd/yyyy	mm/dd/yyyy	Death	1	1
	Placebo	S: XXX	Xx	Xx	Life-threatening	2	2
		P: XX			Hospitalization	3	3
					Disability	4	4
					Congenital Anomaly/Birth Defect	5	5
					Required Intervention to Prevent Permanent Impairment / Damage		
					Other		

Subject ID No.	**SAE**	**Continued Study Participation**	**Study Drug Start Date**	**Date of last administration of study drug prior to SAE**	**SAE Abated after study drug stopped?**	**Continued study drug Administration**	**SAE reappeared after rechallenge?**	**Outcome**
xxx	Verbatim	Yes	mm/dd/yyyy	mm/dd/yyyy	Yes	Yes	Yes	1
		No			No	No	No	2
					n/a		n/a	3

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Outcome: 1=Recovered/Resolved; 2=Recovering/Resolving; 3=Not Recovered/Not Resolved; 4=Recovered/Resolved With Sequelae; 5=Fatal (Date of Death)

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Listing 30: Columbia-Suicide Severity Scale

				Response to Question:												
Subject ID	**Treatment Group**	**Visit Date**	**Study Week**	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**	**Q12**	**Q13**
xxx	Oxytocin	mm/dd/yyyy	1, 2 , 5	Yes	Yes	Yes	Yes	Yes	Yes	Type 1	1	1	0	0	0	Yes
	Placebo		9, 13	No	No	No	No	No	No	Type 2	2	2	1	1	1	No
										Type 3	3	3	2	2	2	
										Type 4	4	4	3	3	3	
										Type 5	5	5	4	4	4	
													5	5	5	

Suicide Ideation

1. Have you wished you were dead or wished you could go to sleep and not wake up?
2. Have you actually had any thoughts of killing yourself?
3. Have you been thinking about how you might do this?
4. Have you had these thoughts and had some intention of acting on them?
5. Have you started to work out or worked out the details of how to kill yourself?
6. Do you intend to carry out this plan?

Intensity of Ideation

7. The following features should be rated with respect to the most severe type of ideation (i.e. 1-5 with 1 being the least severe and 5 being the most severe)
8. How many times have you had these thoughts?1=Less than once a week; 2=Once a week; 3=2-5 times a week; 4=Daily or almost; 5=Many times each day
9. When you have the thoughts, how long do they last? 1=Fleeting-few seconds or minutes; 2=Less than 1 hr-some of the time; 3=1-4 hrs/a lot of time; 4=4-8 hrs/most of day; 5=More than 8 hours/persistent or continuous
10. Could/can you stop thinking about killing yourself or wanting to die if you want to? 1=Easily; 2=Little Difficulty; 3=Some Difficulty; 4=Lot of Difficulty; 5=Unable to control; 0=Does not attempt to control
11. Are there things that stop you from wanting to die or acting on thoughts of committing suicide? 1=Definite deterrents; 2=Probably Deterrents; 3=Uncertain Deterrents; 4=Unlikely Deterrents; 5=No Deterrents; 0=Does not apply
12. What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end pain or stop the way you were feeling or to get attention, revenge or reaction from others 1=Completely to get attention or revenge or reaction; 2=Mostly to get attention or revenge or reaction; 3=Equally to get attention or revenge or reaction and stop pain; 4=Mostly to stop pain; 5=Completely to stop pain; 0=Does not apply

Suicidal Behavior

13. Have you made a suicide attempt?
14. Number of attempts
15. Has the subject engaged in non-suicidal self-injurious behavior?
16. Has there been a time when you started to do something to end your life but someone or something stopped you before actually did anything?
17. Number interrupted
18. Has there been a time when you stared to do something to try to end your life but you stopped yourself before you actually did anything?
19. Number aborted
20. Have you taken any step towards making a suicide attempt or preparing to kill yourself?
21. Suicidal behavior was present during the assessment period
22. Completed suicide?
23. Actual Lethality/Medical Damage; 0=No physical damage; 1=Minor physical damage; 2=Moderate physical Damage; 3=Moderately severe physical damage; 4=Severe physical damage; 5=Death
24. Potential Lethality; 0=Behavior not likely to result in injury; 1=Behavior likely to result in injury, but not death; 2=Behavior likely to result in death

Listing 31: BPAQ Scores

			Scores			
Subject ID	**Treatment Group**	**Week**	**Physical Aggression**	**Verbal Aggression**	**Hostility**	**Anger**
xxx	Oxytocin	xx	xxx	xxx	xxx	xxx
	Placebo					

Listing 32: Blood Chemistries

Subject ID	**Treatment Group**	**Visit Date**	**Test Name**	**Result**	**Units**	**Flag**	**Evaluation**
xxxx	Oxytocin	mm/dd/yyyy	Creatinine	x.xx	mg/dL	H (high)	WNL
	Placebo		Total Bilirubin	xxx	mg/dL	L (low)	Abnormal, NCS
			ALT	xx.x	U/L		Abnormal, CS
			AST	x.xx	U/L		
			sodium	xx.x	U/L		
			Potassium				

Listing 33: Pregnancy Test/Birth Control Data

Subject ID	**Treatment Group**	**Pregnancy Test Performed?**	**Pregnancy Test Date**	**Pregnancy Result**	**Methods of birth control**
xxx	Oxytocin	Not Done	mm/dd/yyyy	Negative	Oral Contraceptive
	Placebo			Positive	Contraceptive Sponge
					Contraceptive Skin Patch
					Double Barrier
					Intrauterine
					Etonogestrel implant
					Medroxyprogesterone
					Complete Abstinence
					Hormonal Vaginal contraceptive Ring
					Surgically Sterile
					Postmenopausal
					Partner surgically Sterile
					Other : xxxxxxxxxxxxxxx

Programming note: Only indicate birth control methods that were indicated as Yes

Listing 34: Blood Alcohol Concentration

Subject ID	Treatment Group	Visit Date	Study Week	BAC Performed	Time of BAC	BAC %
xxx	Oxytocin	mm/dd/yyyy	Screen	Done	hh:mm	x.xxx
	Placebo		1, 2, 3	Not Done		
			4, 6, 8			
			10, 13			

Listing 35: Urine Drug Screen

Subject ID	Treatment Group	Visit Date	Study Week	AMP [a,b]	Benzos	Barb	Coc	Bup	EGT	MDMA	Meth	Methadone	Opioids	Oxy	THC
xxx	Oxytocin	mm/dd/yyyy	Screen	P	P	P	P	P	P	P	P	P	P	P	P
	Placebo		1, 2, 3	N	N	N	N	N	N	N	N	N	N	N	N
			4, 6, 8												
			10, 13												

[a] P=positive; N=negative
[b] AMP=amphetamine, Benzos=benzodiazepines, Coc=cocaine, Meth=methamphetamine, Oxy=oxycodone, Bup=buprenorphine, Barb=barbiturates

Listing 36: Vital Signs and Body Weights

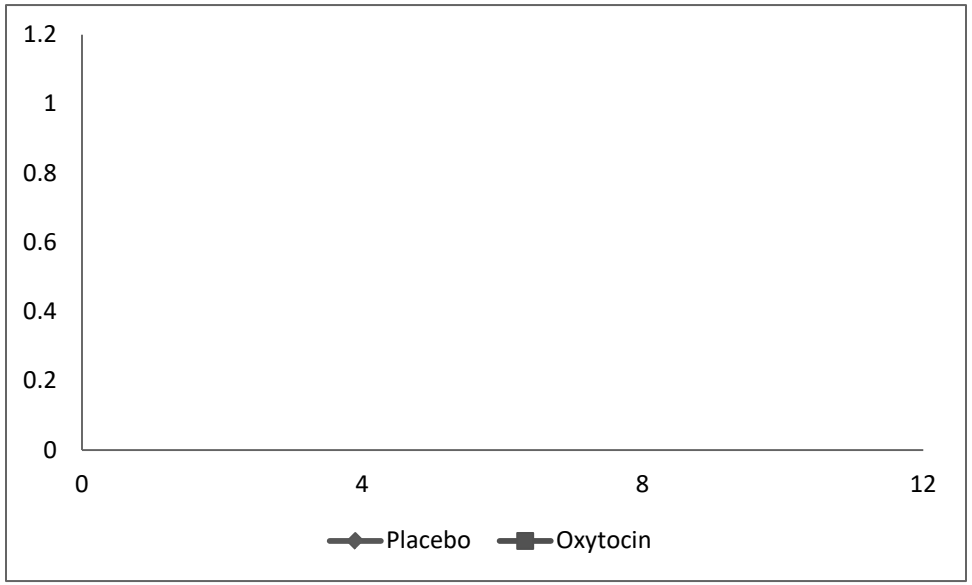
Subject ID	**Treatment Group**	**Visit Date**	**Study Week**	**Weight (Kg)**	**Heart Rate (beats/min)**	**Systolic Pressure (mmHg)**	**Diastolic Pressure (mmHg)**
xxx	Oxytocin	mm/dd/yyyy	Screening	xxx	xxx	xxx	xxx
	Placebo		4				
			8				
			12, 16, 20				
			24, 26, 27				

Listing 37: Prior and Concomitant Medications

Subject ID	**Treatment Group**	**Prior Med?**	**Verbatim Med**	**Indication**	**Route**	**Frequency**	**Dose**	**Start Date**	**Stop Date**	**Continuing?**
xxx	Oxytocin	Yes	xxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	dd/mmm/yyyy	dd/mmm/yyyy	Yes
xxx	Placebo	No	xxx							No

12.3 Figures

Figure 1: Percent Heavy Drinking Days per Week Least Squares Means – Untransformed



*Programmer note: connect the week estimates for each treatment group using linear line join, 95% CI at each estimate, add Cohen's d to each point and * p-value <0.05*

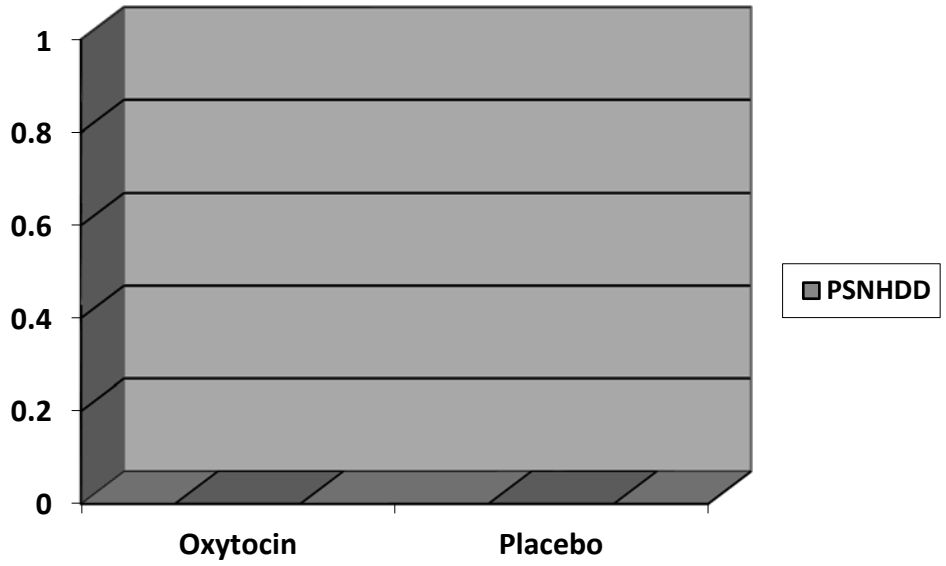
Figure 2: Mean Drinks per Week Least Squares Means – Untransformed

Shell style similar to Figure 1

Figure 3: Mean Drinks per Drinking Day by Week Least Squares Means – Untransformed

Shell style similar to Figure 1

Figure 4: Percentage of Subjects No Heavy Drinking Days Weeks 3-12



*Programmer note: Use percent on y-axis, bar graph of PSNHDD add Cohen's h, * a significant p-value, put values on graph*

Figure 5: Percentage of Subjects Abstinent Weeks 3-12

Shell style similar to Figure 4

Figure 6: Percentage of Subjects with WHO 1-Level Decrease in Alcohol Consumption Weeks 3-12

Shell style similar to Figure 4

Figure 7: Percentage of Subjects with WHO 2-Level Decrease in Alcohol Consumption Weeks 3-12

Shell style similar to Figure 4

Figure 8: Cumulative Grace Periods for Percentage of Subjects No Heavy Drinking Days

Shell style similar to Figure 4

Programmer note put all of the grace periods (full treatment period, 1 month, 2 months) on the same graph

Figure 9: Cumulative Grace Periods for Percentage of Subjects Abstinent

Shell style similar to Figure 4

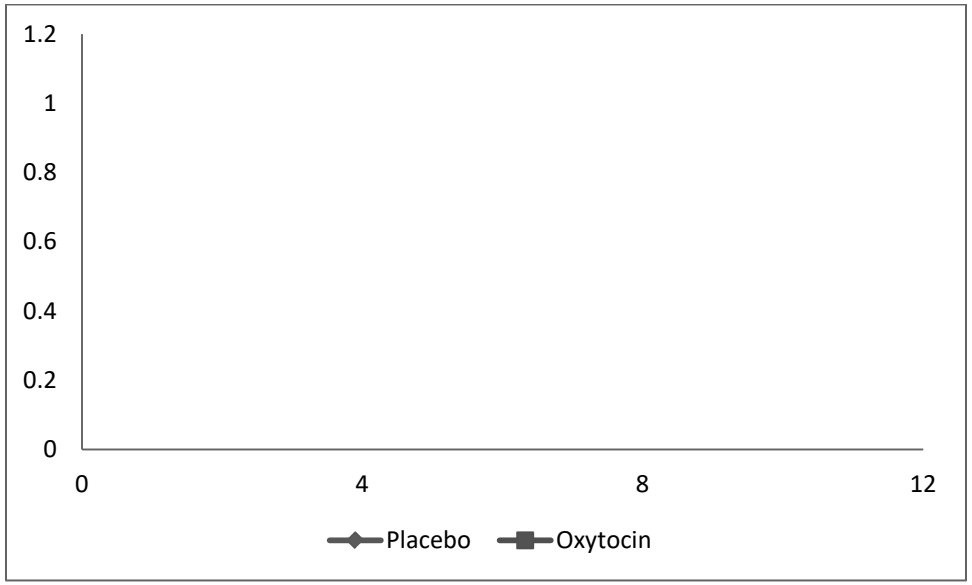
Figure 10: Cumulative Grace Periods for Percentage WHO 1-Level Decrease in Alcohol Consumption

Shell style similar to Figure 4

Figure 11: Cumulative Grace Periods for Percentage WHO 2-Level Decrease in Alcohol Consumption

Shell style similar to Figure 4

Figure 12: Percentage Days Abstinent per Week Least Squares Means – Untransformed



*Programmer note: connect the week estimates for each treatment group using linear line join, add Cohen's d to each point and * p-value <0.05*

Figure 13: Weekly Number of Cigarettes Smoked in Smokers Least Squares Means – Untransformed

Shell style similar to Figure 12

Figure 14: POMS Total Score Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 15: POMS Tension-Anxiety Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 16: POMS Depression-Dejection Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 17: POMS Vigor-Activity Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 18: POMS Fatigue-Inertia Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 19: POMS Anger-Hostility Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 20: POMS Confusion-Bewilderment Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 21: PROMIS Alcohol Negative Consequences Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 22: PROMIS Sleep Disturbances Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 23: PROMIS Pain Interference Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 24: ECR-RS Attachment-Related Anxiety Least Squares Means by Visit – Untransformed

Shell style similar to Figure 12

Figure 25: Clinical Chemistry Values Over Time